OUTCOMES AND DECISION-MAKING IN OLDER ADULTS NEEDING THYROIDECTOMY

by
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Abstract

Over 150,000 thyroidectomies are performed annually in the US, of which 25% are performed in older adults (over 65) (1). Older adults pose unique challenges to surgical decision-making as the benefits of surgery must be weighed against surgical risks, co-existing comorbidities, and postoperative quality of life. While single institution studies demonstrate the safety of thyroidectomy in older adults, population based studies cite increased length of stay and complication rates (2-5). Additionally, prior studies demonstrate that older adults tend to undergo less surgery for thyroid cancer and have worse disease-specific survival (6, 7).

While the dreaded, classic complication of recurrent or superior laryngeal nerve injury is rare, 30-40% of younger adults with intact nerve function still report clinical sequelae of laryngeal dysfunction such as a change in their voice or dysphagia (8-13). It is not well understood why this occurs or who is at risk for developing these changes. Even less is understood about the impact of thyroidectomy on voice, swallowing, and quality of life (QOL) in older adults, despite the likelihood that older adults are at even greater risk than the younger adults who suffer these sequelae**.** While, there are no tools to objectively measure laryngeal muscle mass and strength, frailty, in part a sarcopenia phenotype validated in older adults, might serve as a surrogate marker to predict voice and swallowing impairments following thyroidectomy.

This thesis attempts to advance our understanding of the outcomes and surgical decision-making in older patients undergoing thyroidectomy. The first contribution of this thesis is to evaluate the impact of thyroidectomy on voice and swallowing in older adults using a prospective longitudinal cohort study. The second contribution is to assess the association between frailty and adverse voice and swallowing outcomes post-thyroidectomy. Identifying at-risk older adults for these sequelae is critical for the development of prophylactic and therapeutic interventions to reduce surgical disability in the many older adults who undergo

thyroidectomy. The final contribution of this thesis is to understand surgical decision-making regarding thyroidectomy in older adults utilizing a discrete-choice experiment administered to high-volume endocrine surgeons.

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- **Aarti**

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LIST OF ABBREVIATIONS

BMI: Body Mass Index

DCE: Discrete Choice Experiment

DHI: Dysphagia Handicap Index

GERD: Gastroesophageal Reflux Disease

PTC: Papillary Thyroid Cancer

RLN: Recurrent Laryngeal Nerve

VHI: Voice Handicap Index

CHAPTER 1. Introduction

Over 150,000 thyroidectomies are performed annually in the United States (14). The main indications for a thyroidectomy include presence of a symptomatic, indeterminate or suspicious thyroid nodule, a goiter, Graves' disease, or thyroid cancer (15). Approximately 25% of thyroidectomies are performed on older adults (age ≥ 65) (14). Thyroid nodules are present in 70% of people by the age of 70 (16). Additionally, the incidence of thyroid cancer has doubled over the past couple of decades (17). Furthermore, the U.S. Census Bureau estimates a 58% increase in the population aged ≥ 65 years and an 85% increase in those aged ≥ 85 years by 2035 (18). As life expectancy continues to increase it is expected that 18 million people will turn 65 in the next 10 years (19). Thus, the number of thyroidectomies performed in older adults will continue to rise annually.

However, there is a paucity of data regarding the impact of thyroidectomy in older adults and the existing literature focuses on safety and practice patterns. Although single institution studies demonstrate the safety of thyroidectomy in older patients citing similar complication rates in older and younger individuals, population based studies report higher rates of endocrine-specific and overall complications, in-hospital mortality, unplanned re-admission, costs, and longer mean length of stay (2, 3, 20-22). Population-based studies additionally demonstrate that older patients with thyroid cancer are more likely to undergo less aggressive treatment than that recommended by the American Thyroid Association for all stages of disease (6, 7). The combination of limited and inconsistent data, evolution of treatment guidelines, and surgeon perception have all contributed to significant treatment variation in the management of older patients with surgical thyroid disease. Little is understood regarding methods that surgeons use regarding pre-operative risk assessment and subsequent surgical recommendations in older adults. Surgical decision-making in older adults is complex as surgical complication risks, anesthetic risks, co-existing co-morbidities, and decrement in quality

of life must be weighed against benefits of disease-specific mortality and the possibility of treating an aggressive cancer.

Major thyroid-specific complications including hypoparathyroidism and nerve injury are uncommon even in older patients. Injury to the recurrent laryngeal nerve during thyroidectomy can occur in up to 10% of patients resulting in voice and swallowing alterations (23). Injury to the external branch of the superior laryngeal nerve impairs the production of high tones, and altering the voice's fundamental frequency and ability to project. The larynx, which is innervated by the recurrent laryngeal and superior laryngeal nerves, serves multiple functions including control of respiration, airway protection, coordination of swallowing and phonation. However, despite the infrequent occurrence of nerve injury, 30-40% of younger patients (age 18-65) report sequelae of laryngeal dysfunction including changes in the quality of their voice or dysphagia, which has a significant impact on their quality of life and activities of daily living, but only 7% of these changes persist at 6 months after surgery (8-10, 24, 25). The impact of thyroidectomy on voice, swallowing, and quality of life in older adults who do not have a surgical complication is unknown. Additionally, it is unknown which older adults are at risk of developing these changes.

Voice production requires coordination of three main components: intact myoelastic structures of the larynx for vocal fold vibration, adequate airflow from the respiratory system, and a strong resonating channel including the supraglottic larynx, hypopharynx, nasopharynx, and oral cavity for projection. Deterioration of the cartilaginous and muscular structures of the larynx, decreased pulmonary function, impaired motor neuron function, and intrinsic vocal fold changes can all occur with aging and contribute to presbyphonia (26-29). The larynx also plays a central role in airway protection during swallowing and thus reduced bulk of vocal cords can contribute to aspiration. Aging can cause changes in the structure, motility, coordination, and sensitivity of the swallow process, known as presbyphonia (30). The prevalence of voice

problems in older patients has been reported to range from 6-29% (31-34). Additionally, age-related sarcopenia of the myoelastic structures of the larynx might contribute to older patients being more vulnerable to the violation of surrounding musculature during a thyroidectomy. However, age is associated with a multi-system decline in reserve and may one more susceptible to the stressors of thyroidectomy.

Frailty is a clinically recognizable state of increased vulnerability resulting from age-associated decline in reserve and function across multiple physiologic systems and, is a unique domain and indicator of physiologic reserve characterized by increased vulnerability to unfavorable outcomes, decreased homeostatic reserves and lower resistance to stressor events such as surgery (35, 36). Because it is a condition marked by a decline in multiple physiologic systems leading to increased adverse outcomes from stressors, this construct might be useful to predict patients who are more susceptible to the stress of thyroidectomy and develop voice and swallowing changes after this procedure. The frailty phenotype (shrinking, weakness, exhaustion, low physical activity, slowed walking speed) was first described in a cohort of 5,317 community dwelling older adults (Cardiovascular Health Study, CHS (37). The composite measure has predictive validity for development of, among other adverse events, cardiovascular disease (38), venous thromboembolism (39), disability, hospitalization, and death (40).

In 594 patients undergoing a general surgical procedure, pre-operative frailty phenotype was associated with an increased risk for postoperative complications, length of stay, and discharge to a skilled or assisted living facility (41). There is now considerable literature regarding associations between frailty and adverse outcomes after other surgical procedures, such as kidney transplant. In patients who undergo kidney transplant, frailty is associated with delirium, delayed graft function, longer length of stay, early hospital readmission, lower health-related quality of life, and mortality (42-47). Frailty phenotype has also been associated with including mortality and poor recovery in cardiac surgery (48, 49). Frailty as measured by a modified frailty index was associated with increased per-operative morbidity in common

ambulatory general surgery operations, including hernia, breast, thyroid or parathyroid surgery(50). Frailty as measured by a five-factor modified frailty index was also identified to be predictive of complications after thyroidectomy performed for a multinodular goiter (51). While numerous instrument exist to measure frailty, a frailty phenotype has not been previously used to predict voice and swallowing changes after thyroidectomy. Conversely, the frailty phenotype demonstrated statistically significant differences between voice handicap index (VHI) scores between robust and frail patients when it was measured in 52 community dwelling and 21 assisted living residents (52). Due to the plethora of literature highlighting adverse outcomes after surgery in frail patients and the association between frailty and VHI scores, we hypothesize, that frailty phenotype predicts increased likelihood of developing post-operative adverse voice and swallowing outcomes that impacts patients' quality of life. An improved understanding of the biopsychosocial impact of thyroidectomy on voice and swallowing impairments is critical for informed consent, risk stratification, and peri-operative planning within a population of unique patients who may be at higher risk or may be more affected by these changes.

In Chapter 2, we used a longitudinal, single institution prospective cohort study to assess the incidence of voice and swallowing impairments in older adults after thyroidectomy. We hypothesized that older adults have a higher prevalence of pre-operative voice and swallowing changes and subsequently report higher rates of impairment in voice and swallowing post-thyroidectomy than that reported in the literature for younger adults. Additionally, we hypothesized that most of these impairments resolve by 6-months postoperatively.

In Chapter 3, we investigated the association between frailty and impairments in voice and swallowing and evaluated risk factors associated with these changes. We hypothesized that older adults who are frail or pre-frail are more likely to have pre-operative voice or swallowing alterations and report changes in voice and swallowing compared to those who are robust. We

additionally hypothesized that frail or pre-frail patients who have impairments do not return back to baseline as quickly as those who are robust.

In Chapters 4-5, we investigated how high-volume thyroid surgeons assessed older patients for surgery and how their recommendations changed based on patient age, functional status, and co-morbid conditions. We hypothesized that there is a lack of consistency among surgeons in methods used to assess an older adult's fitness for surgery in addition to recommending lesser extent of surgery as a patient's age increased.

CHAPTER 2.

Patient-Reported Alterations in Voice and Swallowing Post-Thyroidectomy in Older Adults.

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Abstract

Background*:* Despite intact recurrent laryngeal nerves, voice and swallowing complaints are common after thyroidectomy. While the occurrence of these changes has been established in younger patients, the development of these changes in older adults and the impact on their quality of life is unknown. Therefore, the aim of this study was to evaluate the impact of thyroidectomy on alterations in voice and swallowing in older adults.

Materials & Methods*:* We performed an IRB-approved longitudinal prospective cohort study and enrolled older adults seen at a single institution between May 1, 2017 and July 31, 2020. All thyroid procedures were performed with intra-operative nerve monitoring by four high volume surgeons at a single institution. Patients with recurrent laryngeal nerve injury or loss of nerve signal were excluded. Longitudinal assessments were performed utilizing validated surveys including the Voice Handicap Index (VHI) and the Dysphagia Handicap Index (DHI). The incidence and duration of development of impairments in voice and swallowing was examined and differences in mean survey scores were tabulated using a t-test.

Results*:* Of 53 patients undergoing thyroidectomy, 67.9% had abnormal scores on the pre-operative VHI and 77.4% had abnormal scores on the DHI. After thyroidectomy, 49.1% of patients reported worse voice in the early post-operative period and this persisted in 32% of patients at 6 months. After thyroidectomy, 41.5% of patients reported worse swallowing at the initial post-operative visit and this persisted in 32.1% at 6 months.

Conclusions*:* A high prevalence of voice and swallowing impairments exist in older patients. After thyroidectomy there is a high incidence of patient-reported further impairment in voice and swallowing which may persist at 6 months post-operatively. Older patients should be counseled appropriately regarding higher risk of voice and swallowing impairments following thyroidectomy and referred early for therapy.

Introduction

Despite the reported low incidence of temporary or permanent recurrent laryngeal nerve (RLN) injury (0.01–15.4%) and superior laryngeal nerve injury (0.0 – 4.6%), voice and swallowing symptoms after total thyroidectomy are increasingly prevalent (24, 25, 53). Studies including patients with nerve injury report rates of adverse voice and swallowing outcomes of up to 87% with only up to 7% persisting beyond 6 months (53-62). As such, most voice and swallowing impairments following thyroidectomy are not related to demonstrable impaired nerve function.

Prior studies have identified reasons for voice and swallowing impairments including intubation-related trauma, surgical trauma, disruption of the vascular supply and drainage of the larynx, disruption of strap musculature, laryngotracheal fixation with impaired vertical movement, and psychologic reasons (63-66). Although age has not been identified as a risk factor, Papadakis and colleagues demonstrated that patients above 40 years of age suffer from voice changes for a longer duration postoperatively compared to younger patients (67). However the impact of thyroidectomy specifically on older adults (age ≥ 65) is unknown and prior studies were performed on mostly younger adults. Dysphagia and dysphonia after thyroidectomy can significantly impact one's quality of life, affecting social interactions, compliance with medications, and nutritional intake (68).

With increasing age, deterioration of the cartilaginous and myoelastic structures of the larynx can occur and can contribute both to presbyphonia and dysphagia. Atrophy of the upper esophageal sphincter can affect swallowing as well. Thus, aging alone can cause changes in the structure, motility, and coordination of swallowing. Upon retrospective review of 925 patients over the age of 65 undergoing thyroidectomy over a one-year period, 26% of patients reported alteration in voice quality or swallowing. However, almost half of patients were not specifically questioned regarding voice and swallowing alterations in post-operative follow-up and only 24% reported no changes (69). This is likely an underestimate of the true incidence as patients are

likely to under-report changes and they are not typically seen again after the first post-operative visit.

We hypothesize after surgical manipulation older patients are at higher risk of having voice and swallowing changes. Therefore, the aim of the present study is to prospectively assess the incidence of patient-reported voice and swallowing changes following thyroidectomy in the absence of RLN injury.

Material and Methods

Patients were recruited from 4 endocrine surgical clinics at a single institution between May 1, 2017 and July 31, 2020. Demographic and clinical data including risk factors for development of voice or swallowing changes were recorded. Surveys, including the validated Voice Handicap Index (VHI) and Dysphagia Handicap Index (DHI), were administered pre-operatively and at several time points post-operatively including within 4 weeks, at 3 months, and at 6 months. In the VHI (30-items) and DHI (25 items) each item is rated from 0 to 4, with 4 indicating greater impact. The VHI and DHI both have subscales, which, include functional, emotional, and physical. For the VHI, the functional subscale describes the impact of a person's voice disorder on their daily activities. The emotional subscale represents a patient's affective response to a voice disorder, and the physical subscale represents self-perceptions of laryngeal discomfort and voice output characteristics. Similarly, the DHI functional, emotional, and physical subscales attempt to measure the impact of dysphagia on quality of life in each respective area. All thyroid procedures were performed with The Nerve Integrity Monitoring System (NIM, Medtronic, Jacksonville, FL) with endotracheal tube sizes 6.0 or 7.0. Patients were excluded if nerve signal was lost during the procedure, nerve injury during the procedure, or vocal cord immobility documented post-procedure.

Statistical Analysis

Scores for each questionnaire, frequency of complaints, and mean changes pre- and post-operatively at each time point per patient were tabulated. Mean changes (with SD and 95% confidence interval) in scores on each of the surveys post-surgery compared to pre- was calculated to describe the extent and variability of with-in person changes, overall, and by each group including those with and without changes. The difference in survey scores from pre- to post-thyroidectomy was assessed using a paired t-test overall and by each group. The frequency of specific complaints and changes in specific survey questions was also tabulated to characterize what specific aspect of voice or swallowing changed.

Results

Study Population

Approximately 200 patients were approached for enrollment. Of the 70 patients enrolled, 53 older adults completed 6 month follow up (Table 1). The remaining 17 patients have just had surgery, but not enough time for follow up. Of this cohort, the mean age was 71.1 (range 65-94). Majority of patients were female gender (71.7%), of white race (86.8%), and non-smokers (58.5%). Mean BMI of this cohort was 29.8 (range 19.2-48.9). Of this cohort, 13.2% had a history of gastro-esophageal reflux disease (GERD), 28.9% had a prior malignancy, and 11.3% had a Charlson Comorbidity Index of 6 or greater. The most common pre-operative diagnoses included a suspicious thyroid nodule (37.7%), a multinodular goiter (35.9%), and thyroid cancer (13.2%). Regarding the operative procedure performed, 35.9% underwent hemithyroidectomy and 60.4% underwent total thyroidectomy. Final pathology was benign in 54.7% and malignant in 45.3%. Of this cohort, 67.9% had abnormal scores on the pre-operative VHI and 77.4% had abnormal scores on the DHI. Mean pre-operative total VHI score was 7.3 (SD 9.7) and mean pre-operative DHI score was 4.0 (SD 5.3).

Voice

At the pre-operative evaluation, the most frequent positive responses were in the physical and functional subscales. The most frequent positive responses to the physical subscale questions were “The sound of my voice varies throughout the day” reported by 44% followed by “I run out of air when I talk” reported by 34.6%. The most frequent responses were to the functional subscale of questions were “My voice make it difficult for people to hear me” in 37.7%, “People have a difficult time understanding me in a noisy room” in 35.8%, and “My family has difficulty hearing me when I call them throughout the house” in 32.1%. The frequency of these positive responses increased in the initial post-operative period, but went back to baseline by 6 months post-operatively.

In the early post-operative period, there was an increased frequency of responses to physical subscale questions. “The clarity of my voice is unpredictable,” which was reported by 21% pre-operatively, but by 37% in the early post-operative period and by 26.9% at 6 months post-operatively. “My voice is worse in the evening,“ which was reported by 15.4% in pre-operative period, 33.3% in the postoperative period, and 32.1% up to 6 months postoperatively. “My voice ‘gives out’ on me in the middle of speaking” increased from 23% in the pre-operative period to 28% in the initial post-operative period and was reported by 32.7% at 6-months. There was also an increase in positive responses to an emotional subscale question of “I find other people don’t understand my voice problem,” which was reported by 5.6% in the pre-operative period and by 11.2% at 6 months.

Compared to the pre-operative VHI total score, post-operative VHI total scores were higher in 49.1% of patients at the initial post-operative visit, in 43.3% at 3 months, and in 32.1% at 6 months indicating worse function (Figure 1). Compared to the pre-operative assessment, post-operatively in the functional subscale, 47.2% of patients had higher scores early, 39.6% had higher scores at 3 months, and 32.1% had higher scores at 6 months indicating worse

function affecting daily activities (Figure 1). Compared to the pre-operative assessment, post-operatively in the emotional subscale, 30.2% of patients had higher scores early, 35.8% had higher scores at 3 months, and 18.9% had higher scores at 6 months. Compared to the pre-operative assessment, post-operatively in the physical subscale, 47.2% of patients had higher scores early, 43.4% had higher scores at 3 months, and 32.1% had higher scores at 6 months (Figure 1).

In examining differences in mean scores within each subscale at each post-operative time point, only a difference in the physical subscale of voice was seen at one month postoperatively (Table 2). In the physical subscale, the mean score was 4.6 (SD 6.3) postoperatively, compared to 3.07 (SD 5.0) post-operatively ($p = 0.03$). There was no difference in total or other subscale scores for patients at each post-operative time point compared to the pre-operative time point. In summary, voice impairment was common pre-operatively, worsened in the early post-operative period, and 32% of patients reported voice impairments up to 6 months post-operatively. Adverse voice outcomes affected daily activities and how patients heard their voice.

Dysphagia

At the pre-operative evaluation, the most frequent positive responses were in the physical subscale questions. “My mouth feels dry” was reported by 56.6%, “I cannot swallow food without washing it down with liquid” was reported by 45.3%, and “I cough when swallowing liquids” was reported by 43.4%. On the self-reported dysphagia severity scale, 83% of patients noted that their swallowing was normal (score of 1-2) and 17% reported a moderate problem (score 3-5).

After thyroidectomy, the symptoms reported pre-operatively had minimal change. However, patients more frequently reported another physical subscale question of “I cough while eating solid food”, which was reported by 28% pre-operatively, up to 40% in the early post-operative period and dropped back down to 27% at 6 months. Interestingly, emotional

subscale questions of “I am nervous about my swallowing problems” increased from 9.4% baseline to 17.2 early post-operative period back to baseline at 6 months and “I have a fear that I may choke and suffocate with food in the throat because of my swallowing problem” from 17% at baseline to 25.5% early postop to 19% at 6 months. On the self-score, in the early post-operative period, 21.3% reported moderate problem and at 6 months, 10% reported a moderate problem, and 1.9% reported a severe problem.

Compared to the pre-operative DHI assessment, post-operative total DHI scores were higher in 41.5% of patients at the initial post-operative visit, in 43.4% at 3 months, and in 32.1% at 6 months indicating worse function (Figure 2). Compared to the pre-operative assessment, post-operatively in the functional subscale, 35.8% of patients had higher scores early, 37.7% had higher scores at 3 months, and 18.9% had higher scores at 6 months indicating worse function (Figure 2). Compared to the pre-operative assessment, post-operatively in the emotional subscale, 26.6% of patients had higher scores early, 34.0% had higher scores at 3 months, and 17.0% had higher scores at 6 months. Compared to the pre-operative assessment, post-operatively in the physical subscale, 39.6% of patients had higher scores early, 39.6% had higher scores at 3 months, and 32.1% had higher scores at 6 months (Figure 2).

However, no significant differences in mean scores between pre-operative and post-operative scores in the total score, the physical, functional or emotional subscales was observed (Table 3). Therefore, swallowing impairments were prevalent pre-operatively, worsened in the initial post-operative period in all aspects affecting activities of daily living, emotional status, and self-perception of swallowing.

Discussion

To the best of the authors' knowledge, this is the first study to demonstrate that 67.9% and 77.4% of older patients have voice and swallowing impairment prior to thyroidectomy, which worsens post-operatively with changes seen up to 6 months after surgery. Older patients also have a higher frequency of adverse voice and swallowing outcomes both in the early post-operative period as well as at 6 months post-operatively in the absence of intra-operatively documented recurrent laryngeal nerve injury reported by younger patients in prior studies. Prior studies have demonstrated that < 10% of younger patients have persistent voice or swallowing changes at 6 months postoperatively (70). Voice and swallowing impairments persisted in almost 1/3 of patients at 6 months post-operatively and affected performance of daily activities in addition to self-perception.

Our findings of specific voice complaints in the pre-operative periods were consistent with prior studies have demonstrated that voice changes associated with aging include hoarseness and breathiness, vocal fatigue, instability and crackling, while voice amplitude and frequency are preserved (71, 72). The most common responses in the pre-operative period reflected breathiness and vocal instability. Age-related changes associated with dysphagia include reduced bulk and possible increased sensitivity of the vocal cords which was reflected in the high frequency of responses to coughing when drinking liquids (73). This aspect seemed to be exacerbated by thyroidectomy as post-operatively there was a higher frequency of positive responses to coughing when eating solid food, which would imply further increased sensitivity to the vocal cords. Aging also results in lower salivary flow rates, which in combination with certain medications, can lead to xerostomia and was also reflected in the high frequency of responses to the question about dry mouth (73).

The data in the literature assessing the association of voice and swallowing changes after thyroidectomy without RLN injury in relation to age is limited. However, several studies

have described the objective voice and swallowing changes associated with thyroid surgery across all age groups. In a survey completed by 4,426 members of the Thyroid Cancer Survivors' Association, 51% of participants who had undergone thyroidectomies reported postoperative voice disorders, most commonly complaining of hoarseness or a decreased ability to speak loudly, shout, or sing (74). However, this study was unable to clearly identify those patients who may have incurred a nerve injury. In another study by Hong *et al*, acoustic analysis of 54 patients following thyroidectomy without nerve injury showed that speaking fundamental frequencies had been altered and that vocal range had been reduced in 86% of patients (56). A 6 month prospective evaluation of 53 patients undergoing total thyroidectomy without recurrent laryngeal nerve injury attempted to identify a relationship between laryngeal mobility, dysphagia and hoarseness and found no association. Furthermore, 47% of patients reported postoperative swallowing difficulties, most commonly foreign body sensation in the throat. In contrast to our study, the swallowing difficulties and laryngeal mobility impairments resolved in the majority of patients with only 7.6% reporting postoperative swallowing difficulties after 6 months (75).

Similar to our study, a qualitative study of interviews with patients identified a high incidence of dysphagia 2 weeks after thyroidectomy. Two major themes were additionally identified including the concern that dysphagia symptoms produced and discovery of compensatory and coping strategies to mitigate symptoms of dysphagia (76).

As the US population ages, more thyroidectomies will be performed on older adults. The population aged greater than 65 years, reported as 43.1 million or 13.7% of the total population of the United States in 2012, is estimated to double by 2050 to 83.7 million and comprise 20.9% of the total population (77). Additionally, the number of total thyroid nodule related operations has increased from 99,613 in 2006 to 130,216 in 2011, representing a 31% increase in a 5 year period (78). Thus, the number of older patients undergoing total thyroidectomies is expected to grow with time. There is a paucity of data regarding the impact of thyroidectomy on older adults.

The impact of these changes on quality of life is significant (68). Voice and swallowing

alterations have a daily impact on interaction with family and friends, quality of life, participation in society, and difficulty taking medications, which may affect compliance. Furthermore, swallowing difficulties can lead to weight loss, nutritional deficits, and an elevated risk of pneumonia (79, 80). These difficulties may be exaggerated in older adults and can, in turn, increase the risk becoming more vulnerable to stressors. Our study further demonstrated that adverse voice and swallowing outcomes impacted activities of daily living, emotional state of patients, and how patients perceived their own voice and swallowing. Additionally, 32% had impairments at 6 months post-operatively, which is much greater than the 7% reported for younger patients.

Our study has several limitations. Voice and swallowing changes were elicited from surveys and thus recall bias may have affected responses. Reported impairments were analyzed on their presence or absence, however the degree, severity, and duration can vary in quality. There was a lack of standardized objective assessment of voice and swallowing function in all patients. Our sample size limited extensive analysis of risk factors but did demonstrate some trends. There are medications, such as bisphononates, steroids, anticholinergic drugs for urinary retention, and tricyclic anti-depressants and neuroleptics that can exacerbate age-related dysphagia and we did not take those into account. Similarly, we did not factor in prior occupational voice use. Larger studies need to be performed to assess associations between clinical and demographic factors.

In conclusion, post-operative voice and swallowing impairments are prevalent in older patients and there is a high incidence of further impairment of voice and swallowing after thyroidectomy which can persist at 6 months following thyroidectomy. It is imperative to counsel patients regarding this and consider early referral for therapy. Future studies are needed to assess for risk factors and correlation with objective findings.

Table 1. Patient Demographic and Clinical Characteristics (n = 53)

Characteristic	
Mean Age ± SD (range)	71.1 ± 5.7 (65-94)
Female gender	38 (71.7)
Race/Ethnicity	
White	46 (86.8)
Black	6 (11.3)
Other	1 (1.9)
Mean BMI ± SD (range) Kg/m^2	29.8 ±6.6 (19.2-48.9)
Smoking Status	
Current	1 (1.9)
Former	21 (39.6)
Never	31 (58.5)
Gastroesophageal Reflux Disease	7 (13.2)
Prior Malignancy	15 (28.9)
CCI Scores	
2	15 (28.3)
3	13 (24.5)
4	11 (20.8)
5	8 (15.1)
≥6	6 (11.3)
Pre-operative Diagnosis	
Graves' disease	3 (5.7)
Multinodular goiter	19 (35.9)
Thyroid nodule	4 (7.6)
Suspicious thyroid nodule	20 (37.7)
Cancer	7 (13.2)
Pre-operative dysphonia	36 (67.9)
Pre-operative dysphagia	41 (77.4)
Procedure	
Hemithyroidectomy	19 (35.9)
Total thyroidectomy	32 (60.4)
Neck dissection	2 (3.8)
Final Pathology	
Benign	29 (54.7)
Malignant	24 (45.3)

Table 2. Paired t-test for difference in mean post-operative Voice handicap index survey scores compared to pre-operative scores

	Mean scores (SD) n=53	p-value
1 month		
Functional	3.76 (5.7)	NS
Emotional	1.7 (3.5)	NS
Physical*	4.6 (6.3)	0.03
Total	10.1 (14.5)	0.06
3 month		
Functional	3.52 (6.6)	NS
Emotional	1.8 (5.7)	NS
Physical	4.3 (6.8)	NS
Total	9.6 (17.9)	NS
6 months		
Functional	3.71 (6.9)	NS
Emotional	1.8 (5.1)	NS
Physical	4.2 (7.2)	NS
Total	9.7 (18.3)	NS

Table 3. Paired t-test for difference in mean post-operative dysphagia handicap index survey scores compared to pre-operative scores

	Mean scores (SD) n=53	p-value
1 month		
Functional	1.5 (2.9)	NS
Emotional	0.7 (1.8)	NS
Physical	2.9 (2.8)	NS
Total	5.1 (6.7)	NS
3 month		
Functional	0.7 (1.7)	NS
Emotional	0.3 (0.8)	NS
Physical	2.0 (2.3)	NS
Total	3 (1.8)	NS
6 months		
Functional	0.7 (1.4)	NS
Emotional	0.3 (0.8)	NS
Physical	2.3 (1.6)	NS
Total	3.3 (4.0)	NS

NS = non-significant

Figure 1. Percentage of patients with change by at least one point (worse, improved, no change) in voice as reflected by Voice Handicap Index (VHI) scores within 4 weeks, 3 months, and 6 months post-operatively compared to pre-operative assessment (n=53).

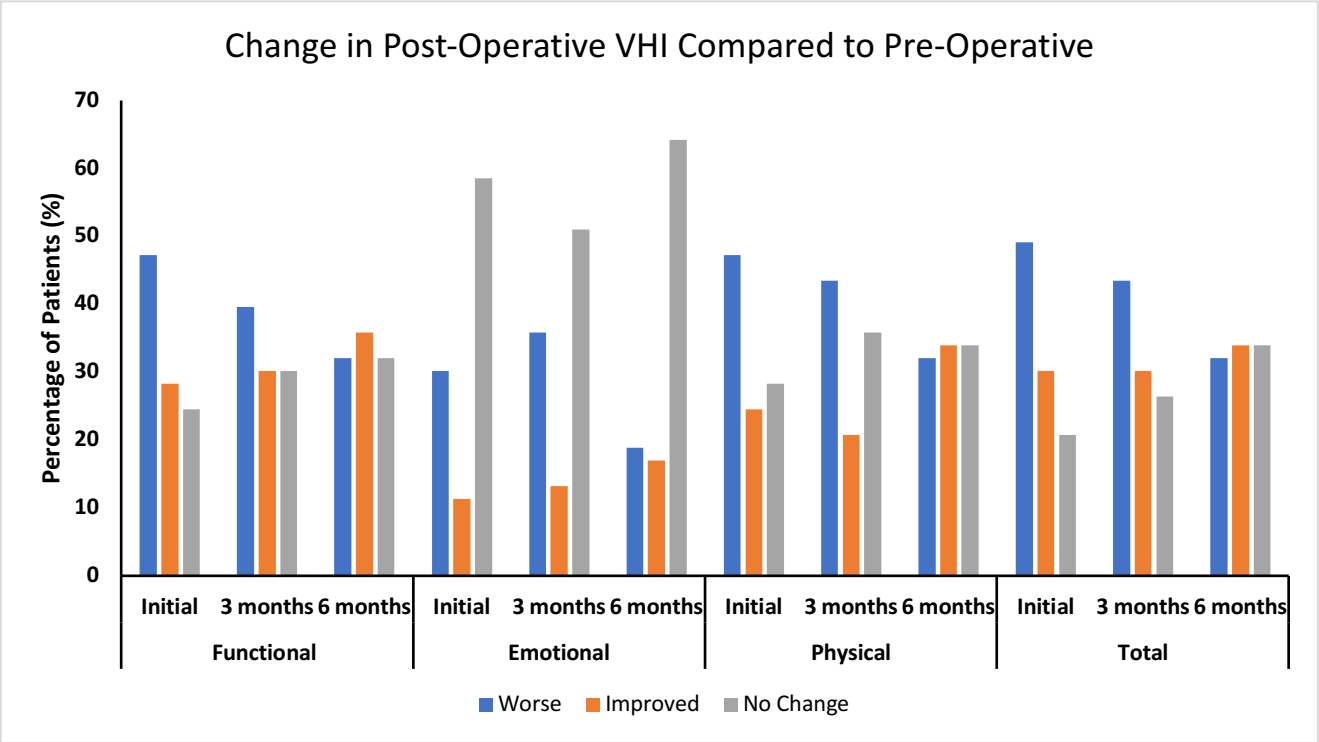
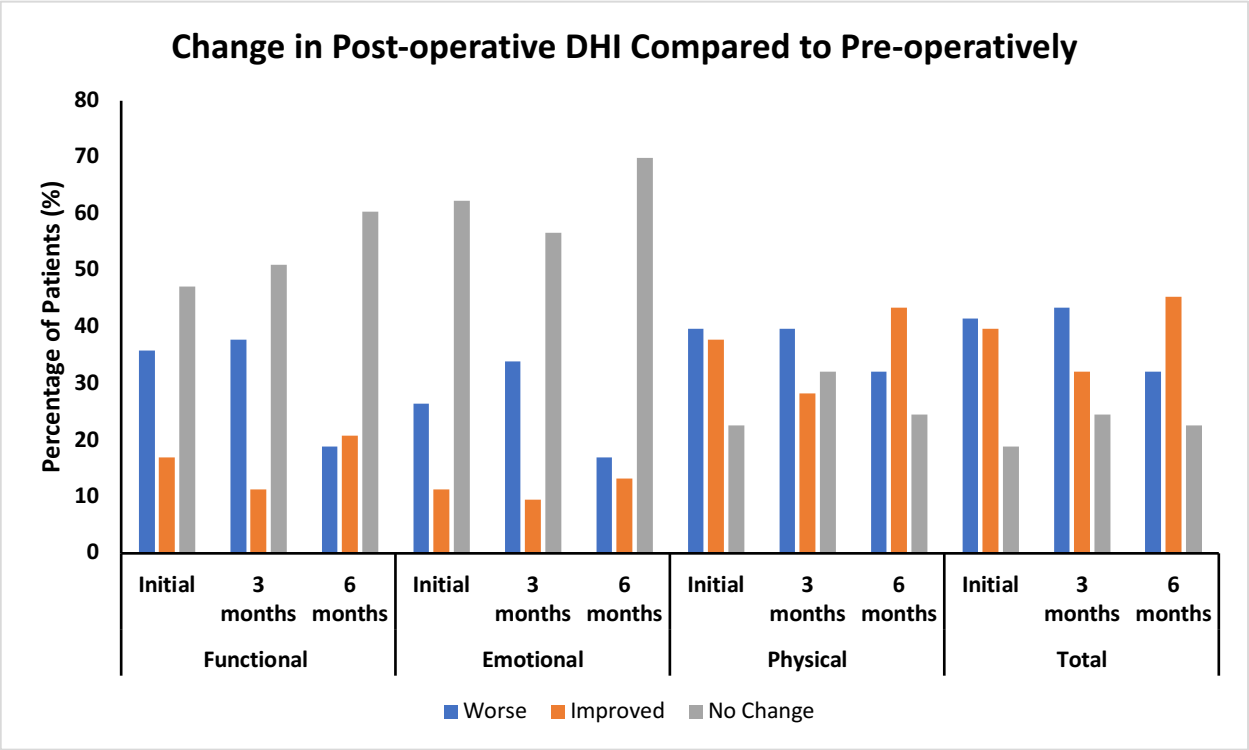


Figure 2. Percentage of patients with change (worse, improved, no change) in swallowing as reflected by change in Dysphagia Handicap Index (DHI) scores within 4 weeks, 3 months, and 6 months post-operatively compared to pre-operative assessment (n=53).



CHAPTER 3.

Association between Frailty and Post-thyroidectomy alterations in Voice and Swallowing

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Abstract

***Background**:* Older adults experience a high incidence of adverse voice and swallowing outcomes after thyroidectomy. The association between frailty status and these changes is unknown. The aim of this study was to evaluate the association between frailty on the incidence of voice and swallowing alterations after thyroidectomy.

***Materials & Methods**:* We performed an IRB-approved prospective longitudinal cohort study among older patients undergoing thyroid surgery between January 2014 and September 2016. Patients with RLN injury were excluded. Frailty was assessed using the Fried Frailty Phenotype at the initial pre-operative visit. Validated surveys including the Voice Handicap Index (VHI) and Dysphagia Handicap Index (DHI) were administered up to 6 months postoperatively. The association among risk factors, including frailty status, prior history of neck surgery, frequent voice use, presence of malignancy or gastroesophageal reflux disease, and smoking status and reported voice and/or swallowing changes was examined. Frailty was defined as frail or pre-frail.

***Results**:* Of 70 patients enrolled, 53 completed 6 months of follow up. Of this cohort, 21 patients (39.6%) were robust, 27 (51.0%) were pre-frail, and 5 (9.4%) were frail. Voice or swallowing impairments were reported by 8 (38.1%) robust patients compared to 23 (71.8%) frail patients in the initial post-operative period (p=0.015) and by 6 (28.6%) robust patients compared to 20 (62.5%) frail patients up to 6 months post-operatively (p=0.016). Compared to robust patients, frail patients had a 3.65 increased odds (95%CI: 1.12-11.90) of developing a functional and physical voice change in the initial post-operative period and a 4.7 increased odds (95% CI: 1.14-19.07) at 6 months in the physical subscale. Compared to robust patients, frail patients had 3.75 increased odds (95% CI: 1.03-13.65) of developing functional swallowing impairments in the early post-operative period. Body mass index (BMI) and malignant pathology were also identified as risk factors for developing voice and swallowing changes respectively.

***Conclusions**:* Frailty may be associated with increased voice and swallowing impairments after thyroidectomy, however larger studies are needed to adequately identify risk factors for voice and swallowing impairments post-thyroidectomy.

Introduction

Over 150,000 thyroidectomies are performed annually in the United States and approximately 25% of thyroidectomies are performed on older adults (age ≥ 65) (14). The main indications for a thyroidectomy include presence of a symptomatic, indeterminate or suspicious thyroid nodule, a goiter, Graves' disease, or thyroid cancer (15). Thyroid nodules are present in 70% of people by the age of 70 (16). Additionally, the incidence of thyroid cancer has doubled over the past couple of decades. Furthermore, the U.S. Census Bureau estimates a 58% increase in the population aged ≥ 65 years and an 85% increase in those aged ≥ 85 years by 2035 (ref). Thus, the number of thyroidectomies performed in older adults will continue to rise annually.

While overall complication rates are low, older adults undergoing thyroidectomy have a high incidence of voice and swallowing impairments following thyroidectomy despite intact laryngeal nerves. Possible reasons for this may be due to violation of the strap muscles, manipulation of the cricothyroid muscles, and scarring in the laryngo-tracheal region. Risk factors that have been identified in prior studies for developing postoperative changes in voice or swallowing include presence of gastroesophageal reflux disease (GERD), frequent voice use, smoking history, prior neck surgery, and arytenoid trauma due to endotracheal intubation (53, 59, 81, 82). Although several studies have evaluated risk factors for adverse voice and swallowing outcomes, older adults represent a unique and under-represented population. Deterioration of the cartilaginous and muscular structures of the larynx that occur normally with aging can contribute to changes in voice in addition to changes in the structure, motility, coordination, and sensitivity of the swallow process (30). These changes may also make one more susceptible to surgical manipulation and thus should be assessed as a risk factor for developing impaired voice and swallowing post-thyroidectomy

Frailty is a unique domain and indicator of physiologic reserve characterized by increased vulnerability to unfavorable outcomes, decreased homeostatic reserves and lower

resistance to stressor events such as surgery (35, 36). The frailty phenotype (shrinking, weakness, exhaustion, low physical activity, slowed walking speed) was first described in a cohort of 5,317 community dwelling older adults (Cardiovascular Health Study, CHS (37). It is in part a sarcopenia phenotype. The composite measure has predictive validity for development of, among other adverse events, cardiovascular disease (38), venous thromboembolism (39), disability, hospitalization, and death (40). Furthermore, in 594 patients undergoing a general surgical procedure pre-operative frailty was associated with an increased risk for postoperative complications, length of stay, and discharge to a skilled or assisted living facility (41). Multiple studies have been published citing the association between frailty and poor outcomes after surgery, specifically transplant surgery, general surgical procedures, and cardiac procedures. For example, frail patients who undergo kidney transplant, are more likely to experience post-operative delirium, delayed graft function, longer length of stay, early hospital readmission, lower health-related quality of life, and mortality (42-47). Frailty patients who undergo cardiac procedures have higher mortality and poor recovery (48, 49). In common general surgery operations, including thyroidectomy, frailty as measured by a modified frailty index was associated with increased per-operative morbidity (50). Frail patients are also noted to have higher voice handicap index (VHI) scores when compared to robust patients (52). However, use of this phenotype to predict which patients are more likely to develop post-operative adverse swallowing and voice outcomes after thyroidectomy has not yet been performed even though frailty is associated with worse outcomes after surgery and with presbyphonia.

Therefore the main objective of this study is to evaluate the association between frailty and incidence of post-operative alterations in voice and swallowing post-thyroidectomy.

Methods

Patients were recruited from 4 endocrine surgical clinics at a single institution between May 1, 2017 and July 31, 2020. Demographic and clinical data was collected and recorded.

Surveys were administered pre-operatively and at several time points post-operatively including within 4 weeks, at 3 months, and at 6 months. Administered surveys included the validated Voice Handicap Index (VHI) and Dysphagia Handicap Index (DHI). In the VHI (30-items) and DHI (25 items) each item is rated from 0 to 4, with 4 indicating greater impact. A voice or swallowing impairment was defined as any increase in score on the VHI or DHI respectively.

Frailty Assessment

Frailty as defined by Fried et al., was measured using a previously validated scale evaluating 5 binary criteria and calculated using the Hopkins frailty calculator (http://www.johnshopkinssolutions.com/solution/frailty/). Individuals with >=3 criteria are designated as “frail”, 1-2 as “pre-frail,” and 0 as “robust”.

Statistical Analysis

Frailty, average total and subscale VHI and DHI survey scores, and change in survey scores were assessed with a Mann Whitney U test. Frailty phenotype was dichotomized to robust versus pre-frail or frail. A Pearson’s chi-squared or Fisher’s exact was used to evaluate an association between voice or swallowing changes overall (present or absent) and in each subscale and frailty status. Mann Whitney U test was used to examine difference in mean scores by frailty status. Logistic regression model was used to examine risk factors, including age, sex, BMI, presence of GERD, smoking status, extent of thyroid procedure (hemithyroidectomy versus total thyroidectomy), thyroid pathology, and frailty status for increased scores on total and subscale VHI and DHI indicating worse function. Age and BMI were treated as both a continuous variable and categorical variables with age dichotomized into < 75 years and >=75 and BMI dichotomized to non-obese (BMI<30 kg/m^2) or obese (BMI>= 30 kg/m^2).

RESULTS

Study Population

Of the 70 patients enrolled, 53 older adults completed 6 month follow up. The age range was 65-94 (mean age was 71.1). Most patients were female gender (71.7%), as expected with thyroid disease and of white race (86.8%). The majority of patients were non-smokers (58.5%), non-obese (58.5%), with a Charlson comorbidity index of <6 (88.7%) and did not have a history of gastro-esophageal reflux disease (GERD) or prior malignancy. The most common pre-operative diagnoses included a suspicious thyroid nodule (37.7%), a multinodular goiter (35.9%), and thyroid cancer (13.2%). Most patients underwent total thyroidectomy (60.4%) and most had benign final pathology (54.7%). Majority of patients had abnormal scores on the pre-operative VHI (67.9%) with mean score of 7.3 (SD 9.7). Majority of patients also had abnormal scores on the pre-operative DHI (77.4%) with mean pre-operative DHI score of 4.0 (SD 5.3).

Patient Characteristics by Frailty Status

Regarding the frailty phenotype, 21 patients (39.6%) were robust, 27 (51.0%) were pre-frail, and 5 (9.4%) were frail (Table 1). The majority of pre-frail/frail individuals in the sample, as compared to robust, were female, of white race, non-smokers, and had a mini-cognitive score of 3-5. Both groups had similar mean age and mean BMI. Among robust patients, the most common diagnoses were a suspicious thyroid nodule in 52.4% followed by a multinodular goiter in 33.3%, whereas in the non-robust group, the most common diagnoses were a multinodular goiter in 37.5% followed by a suspicious nodule in 28.1% (Figure 1). At baseline, abnormal VHI scores were present in 57% of robust patients and 75% of frail patients, and abnormal DHI scores were present in 67% of robust patients and 84% of frail patients.

Voice or Swallowing Impairments Post-thyroidectomy by Frailty Phenotype

Of this cohort, 8 (38.1%) robust patients compared to 23 (71.8%) frail patients had higher VHI or DHI scores in the initial post-operative period (p=0.015). At 6-months post-

thyroidectomy, 6 (28.6%) of robust patients versus 20 (62.5%) of frail patients had voice or swallowing impairments (p=0.016). In the initial post-operative period, the greatest differences in voice impairments between frailty phenotypes were seen in the functional and physical subscales with 6 (28.7%) of robust patients compared to 19 (59.4%) frail patients reporting voice impairments for each of the subscales (p=0.028) (Figure 2a). The difference between frailty phenotypes for the physical subscale of voice persisted at 6 months with 3 (14.3%) robust patients compared to 14 (43.5%) frail patients reporting worse function in this domain (p=0.025). Regarding swallowing dysfunction, in the initial post-operative period, the greatest differences between frailty phenotypes was seen in the functional subscale with 4 (19.1%) robust patients and 15 (46.9%) frail patients reporting impairment (p=0.046). At 6 months, no significant differences were seen between frailty phenotypes in dysphagia handicap index total or subscale scores (Figure 2b).

Association between Frailty and Voice Impairments Post-thyroidectomy

Comparing robust to nonrobust patients, 33.3% versus 59.3% reported worse scores in the early post-operative period (p=0.06) whereas 19.1% compared to 40.6% reported worse scores at 6 months (p=0.100). On univariate logistic regression, compared to robust patients, frail patients had a 3.65 increased odds (95%CI: 1.12-11.90) of having a worse score in the functional subscale of voice in the early post-operative period compared to the pre-operative period indicating a change in daily activities due to voice (Table 3a). Frail patients had a 3.65 increased odds (95% CI:1.12-11.90) in the initial post-operative period and a 4.7 increased odds (95% CI: 1.14-19.07) 6 months post-operatively of having a worse score compared to pre-operative in physical subscale of voice, indicating that this impairment influenced self-perception (Table 3b). Frailty was not significantly associated worsening of total VHI scores in the early postoperative period (OR=2.92, 95% CI:0.93-9.22) or at 6 months postoperatively (OR= 2.91 95% CI: 0.79-10.65).

In evaluating risk factors for developing voice changes in the early post-operative period, increasing BMI was associated with a 1.11 increased odds (95% CI: 1.01-1.22) of developing voice changes (Table 2). Age, sex, race, GERD, smoking status, procedure, final pathology, pre-operative dysphagia, pre-operative dysphonia were not associated with developing voice changes post-operatively. An exploratory model with frailty, age, and sex was performed an the association between frailty and changes was attenuated.

Association between Frailty and Swallowing Impairments Post-thyroidectomy

In the early post-operative period, 28.5% of robust patients compared to 50% of frail patients reported worse scores. At 6 months post-operatively, 19.1% of robust patients compared to 43.8% of frail patients reported worse scores at 6 months (Figure 2b). In the early post-operative period, 19.1% of robust and 46.9% of frail patients felt that the swallowing change impacted their daily activities (p=0.039) and at 6 months post-operatively, 4.8% robust and 9% of frail patients felt that their swallowing impairment affected their daily activities (p=0.069) . Compared to robust patients, frail patients had 3.75 increased odds (95% CI: 1.03-13.65) of developing swallowing impairments that impacted their daily activities as indicated by worse score on the functional subscale in the early post-operative period, however, this association dissipated at 6-months postoperatively. Frailty was not associated with impaired swallowing overall or in the physical or emotional subscales in the early or late post-operative periods.

In evaluating risk factors for developing swallowing impairments in the early post-operative period, age, sex, race, GERD, smoking status, frailty, procedure, final pathology, pre-operative dysphagia, pre-operative dysphonia were not associated with developing any swallowing impairments (Table 3). However, at 6 months post-operatively patients with malignant final pathology had 4.8 increased odds (95%CI: 1.37-16.79) of developing swallowing impairments at 6 months postoperatively.

Discussion

To the authors' knowledge, this is the first prospective longitudinal study to assess the association between frailty and post-thyroidectomy impairments in voice and swallowing. Frail patients reported voice and swallowing impairments both in the early postoperative period as well as up to 6 months post-operatively 20-30% more frequently than robust patients. Frail patients had a 3.65 increased odds (95% CI:1.12-11.90) in the initial post-operative period and a 4.7-fold increased odds (95% CI: 1.14-19.07) 6 months post-operatively of developing an alteration in physical subscale voice and a 3.75 increased odds (95% CI: 1.03-13.65) of developing swallowing impairments that impacted their daily activities as indicated by worse score on the functional subscale in the initial post-operative period.

Voice impairments can have adverse effects on activities or functioning in daily life, emotional consequences, and in physical domains of a patient's quality of life. Prior studies performed predominantly in younger patients have documented voice impairment after thyroid surgery in up to 40% of patients without any nerve injury. Other studies have identified risk factors for voice impairment including age of 45-54 years, Black or Asian race, presence of GERD, or malignant pathology (83). In a study by Akyildiz and colleagues of 36 patients who underwent thyroidectomy, females and males had different degrees of deterioration and amelioration of acoustic voice parameters (84). Similar to our study, another study of 54 patients found that the above risk factors did not predict post-operative voice changes, but only a voice change at the initial post-operative appointment predicted a voice change at 3 months (66).

Voice intensity is known to decrease with age due to atrophy of the cartilaginous and muscular structures that support the larynx and increasing age may be associated with higher VHI scores (85). Of our population, 67% reported a voice impairment prior to surgery, however, there was no association between age or frailty with preoperative voice impairment. Additionally, pre-operative voice impairment was not a risk factor for post-operative voice impairment. Voice changes following thyroid surgery are likely underrecognized likely in part due to limited use of

scales for ascertainment. The etiology of voice impairment is also unclear but may include dissection of the overlying strap musculature, laryngeal irritation or edema from airway management, or scar tissue formation.

This dissection may similarly lead to dysphagia or alterations in swallowing post-thyroidectomy. Prior studies in predominantly younger patients have demonstrated that retained boluses of food or impaired swallowing in approximately 40% after thyroidectomy (86-89). In contrast to our study, the major risk factor for post-operative swallowing impairment that has been identified in a prior study includes presence of GERD, which is associated with decreased laryngopharyngeal sphincter pressure (90). Our study did not demonstrate an association between GERD and adverse swallowing outcomes post-thyroidectomy. The only other risk factor that was previously identified in a retrospective review was age >50 (69). We additionally identified that malignant pathology was associated with swallowing impairments. While the etiology for this is not completely clear, it may be due to increased dissection.

The increased dissection around the muscular and cartilaginous larynx may be less tolerated by older patients who have an atrophied support structure. Frailty, in part a sarcopenia phenotype, may be used to help predict which patients would be more susceptible to these changes. The understanding of the association between frailty and adverse outcomes in older patients undergoing the stress of surgery has significantly expanded in the past decade. Studies have demonstrated that frail older patients experience increased complication rates and prolonged recovery after a wide range of elective, emergent, and common ambulatory surgical procedures(50, 91-95). However, our study is the first to demonstrate that voice and swallowing changes post-thyroidectomy, which may arise in part due to laryngeal muscle dissection, are increased in frail patients and affect their ability to function in daily activities in addition to alter self-perception up to 6 months postoperatively.

Our study has several limitations including our sample size and lack of objective assessments to correlate to subjective findings. Multiple thyroid pathologies were included and

we also included both hemi- and total thyroidectomies. However, extent of surgery was not associated with developing voice or swallowing impairments. There was also a selection bias in that patients were recruited from surgical clinics and some patients may have never been referred to surgery. Our sample size limited the ability to adequately test if an association between frailty and voice or swallowing changes persists after age adjustment. Future studies with a larger sample size, objective assessments, longer follow-up with testing associations between specific aspects of the phenotype, and assessment of sex and frailty interactions, are needed to further elucidate the duration and intensity of these changes, ascertain risk factors, and identify interventions to mitigate these outcomes. In summary, pre-frailty/frailty is associated with adverse voice and swallowing outcomes post-thyroidectomy that can affect an older patients quality of life.

Tables

Table 1. Patient Demographic and Clinical Characteristics by Frailty Phenotype

Characteristic	Robust (n= 21)	Pre-Frail/Frail (n= 32)
Age (mean SD) in years	70.6 ± 4.7 (65-83)	71.4 ± 6.3 (65-94)
Female	11 (52.3)	27 (84.4)
Race		
White	17 (81)	29 (90.6)
Black	3 (14.3)	3 (9.4)
Other	1 (4.7)	0 (0)
BMI (Kg/m^2)	29.7 ± 5.7	30.0 ± 7.1
Smoking		
Current	1 (4.8)	0 (0)
Former	8 (38.1)	13 (40.6)
Never	12 (57.1)	19 (59.4)
GERD	3 (14.3)	4 (12.5)
Prior Malignancy	5 (23.8)	10 (31.3)
Mini-cognitive Score		
2	0 (0)	1 (3.1)
3-5	21 (100)	31 (96.9)
Pre-operative Diagnosis		
Graves' disease	0 (0)	3 (9.4)
Thyroid cancer	2 (9.5)	5 (15.6)
Multinodular goiter	7 (33.3)	12 (37.5)
Thyroid nodule	1 (4.8)	3 (9.4)
Suspicious nodule	11 (52.4)	9 (28.1)
Malignant Final Pathology	10 (47.6)	14 (43.8)
Pre-operative dysphonia	12 (57)	24 (75)
Pre-operative dysphagia	14 (66.7)	27 (84.4)

Table 2. Difference in mean survey scores by frailty phenotype assessed by Mann Whitney U test

	Robust (n = 21)	Pre-Frail/Frail (n = 32)	p-value
Voice			
Preoperative			
Functional	3.2 (3.4)	3.2 (4.0)	0.3919
Emotional	0.7 (2.2)	1.4 (2.9)	0.3076
Physical	1.9 (2.4)	4.4 (5.6)	0.0855
Total	4.9 (5.8)	8.9 (11.3)	0.1797
1 month			
Functional*	1.1 (4.9)	4.8 (6.1)	0.0404
Emotional	1.0 (1.9)	2.3 (4.3)	0.4066
Physical	3.1 (5.5)	5.8 (6.6)	0.0506
Total*	6.5 (11.7)	12.8 (16.1)	0.0127
3 month			
Functional*	1.1 (2.2)	5.1 (7.9)	0.0171
Emotional*	0.2 (0.8)	2.8 (7.1)	0.0350
Physical*	1.8 (3.0)	5.8 (8.1)	0.0415
Total*	3.2 (5.0)	13.7 (21.7)	0.0237
6 months			
Functional*	1.1 (2.2)	5.5 (8.4)	0.0227
Emotional	0.6 (2.1)	2.7 (6.3)	0.0598
Physical*	1.6 (4.1)	6.0 (8.3)	0.0084
Total*	3.2 (7.5)	14.1 (21.9)	0.0133
Dysphagia			
Preoperative			
Functional*	0.2 (0.5)	1.4 (2.5)	0.0288
Emotional	0.1 (0.4)	0.6 (0.2)	0.0376
Physical*	1.6 (2.0)	3.4 (3.1)	0.0193
Total*	1.9 (2.6)	5.4 (6.1)	0.0085
1 month			
Functional	0.8 (1.8)	2.0 (3.4)	0.0446
Emotional	0.5 (1.3)	0.9 (2.0)	0.3031
Physical*	1.8 (2.3)	3.7 (2.9)	0.0123
Total	3.1 (5.1)	6.6 (7.7)	0.0166
3 month			
Functional*	0.1 (0.3)	1.1 (2.0)	0.0217
Emotional	0.1 (0.3)	0.5 (0.9)	0.0920
Physical	1.4 (1.8)	2.4 (2.5)	0.2134
Total	1.5 (1.9)	3.9 (4.7)	0.0664
6 months			
Functional*	0.04 (0.2)	1.1 (1.8)	0.0042
Emotional	0.1 (0.3)	0.4 (1.0)	0.1797
Physical*	1.2 (1.7)	3.1 (2.6)	0.0026
Total*	1.3 (1.9)	4.7 (4.4)	0.0012

Table 3a. Unadjusted associations between patient factors and increased VHI score early (within 4 weeks) post-thyroidectomy.

Patient and Clinical Factors	Total Score OR (95% CI)	Functional OR (95% CI)	Physical OR (95% CI)
Age	1.04 (0.94-1.14)	1.07 (0.97-1.19)	1.05 (0.95-1.16)
Sex	0.40 (0.12-1.41)	0.18 (0.04-0.75)	0.45 (0.13-1.57)
Race	1.04 (0.28-3.9)	0.70 (0.18-2.75)	1.11 (0.30-4.16)
BMI	**1.11 (1.01-1.22)***	**1.12 (1.01-1.23)**	1.06 (0.97-1.16)
Smoking status	0.78 (0.26-2.34)	0.65 (0.22-1.96)	2.29 (0.32-7.90)
GERD	2.97 (0.52-16.95)	3.25 (0.57-18.52)	1.59 (0.32-7.90)
Procedure	2.12 (0.69-6.87)	1.93 (0.61-6.09)	2.74 (0.84-8.93)
Final pathology	0.79 (0.27-2.34)	1.23 (0.42-3.64)	0.91 (0.31-2.68)
Frail Phenotype	2.92 (0.9-9.2)	**3.65 (1.12-11.90)**	**3.65 (1.12-11.90)**
Pre-operative dysphonia	1.1 (0.3-3.5)	1.43 (0.45-4.58)	2.04 (0.62-6.74)
Pre-operative dysphagia	1.5 (0.4-5.4)	2.1 (0.55-8.08)	2.1 (0.55-8.08)

Table 3b. Unadjusted associations between patient factors and increased VHI score 6 months post-thyroidectomy.

Patient and Clinical Factors	Total Score OR (95% CI)	Functional OR (95% CI)	Physical OR (95% CI)
Age	0.95 (0.85-1.07)	0.95 (0.84-1.06)	1.0 (0.90-1.11)
Sex	1.43 (0.38-5.39)	2.33 (0.56-9.71)	4.2 (0.84-21.5)
Race	1.25 (0.32-4.88)	1.24 (0.32-4.89)	0.73 (0.16-3.38)
BMI	0.99 (0.90-1.08)	1.04 (0.95-1.13)	1.01 (0.93-1.10)
Smoking status	1.01 (0.56-1.84)	1.01 (0.56-1.84)	4.23 (0.84-21.6)
GERD	1.71 (0.34-8.69)	3.38 (0.66-17.25)	0.83 (0.14-4.77)
Procedure	2.32 (0.63-8.53)	3.73 (0.91-15.29)	1.53 (0.44-5.28)
Final pathology	1.11 (0.35-3.53)	1.11 (0.35-3.53)	0.78 (0.24-2.51)
Frail Phenotype	2.91 (0.79-10.65)	2.91 (0.79-10.65)	**4.67 (1.14-19.07)**

Table 4. Exploratory age and sex adjusted associations between patient factors and early (within 4 weeks) voice impairment post-thyroidectomy

	Total Score	Functional Subscale
Frail Phenotype	2.45 (0.68-8.79)	2.60 (0.66-10.22)
BMI	1.11 (1.01-1.24)	**1.15 (1.02-1.29)**
Age	1.03 (0.97-1.16)	1.11 (0.96-1.30)
Sex	0.43 (0.10-1.78)	0.12 (0.02-0.71)

Table 5. Unadjusted associations between patient factors and early (within 4 weeks) swallowing impairment post-thyroidectomy

Patient Factors	**Total Score OR (95% CI)**	**Functional OR (95% CI)**	**Physical OR (95% CI)**
Age	1.02 (0.93-1.12)	0.96 (0.86-1.07)	1.02 (0.93-1.12)
Sex	0.92 (0.27-3.10)	0.86 (0.24-3.0)	1.02 (0.30-3.46)
Race	1.37 (0.36-5.17)	1.71 (.45-6.53)	0.92 (0.24-3.61)
BMI	1.01 (0.93-1.10)	0.96 (0.87-1.05)	1.0 (0.92-1.09)
Smoking status	1.82 (0.60-5.54)	2.04 (0.65-6.39)	1.5 (0.50-4.63)
GERD	1.07 (0.21-5.32)	1.04 (0.28-7.07)	0.57 (0.10-3.25)
Frailty	2.50 (0.77-8.08)	**3.75 (1.03-13.65)**	3.2 (0.94-10.84)
Procedure	2.8 (0.83-9.5)	**4.74 (1.16-19.32)**	2.49 (0.73-8.46)
Final pathology	2.63 (0.85-8.08)	**4.53 (1.36-15.12)**	2.22 (0.72-6.83)
Dysphonia	1.47 (0.45-4.83)	1.53 (0.44-5.28)	1.31 (40-4.33)
Dysphagia	1.0 (0.27–3.66)	1.92 (0.45-8.18)	0.90 (0.24-3.31)

Table 6. Exploratory age and sex adjusted association between patient factors and early (within 4 weeks) swallowing impairment post-thyroidectomy

	Overall Score OR (95% CI)	Functional Subscale OR (95% CI)
Frail Phenotype	2.80 (0.73-10.65)	**6.35 (1.22-32.89)**
Malignant pathology	2.88 (0.88-9.45)	**5.84 (1.50-22.70)**
Age	1.02 (0.92-1.13)	0.94 (0.83-1.06)
Sex	1.07 (0.26-4.48)	1.39 (0.29-6.81)

Figures

Figure 1. Thyroid diagnoses stratified by frailty phenotype.

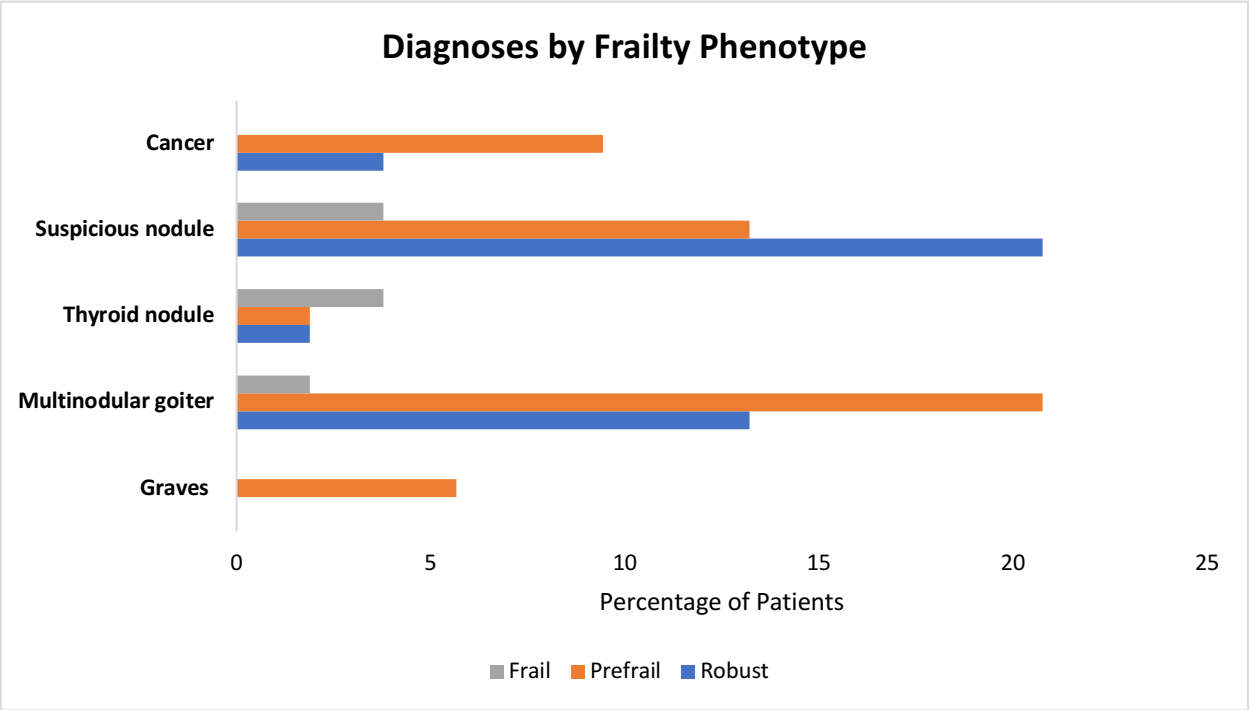


Figure 2a. Percentage of patients with worse Total Voice Handicap Index scores post-operatively compared to preoperatively by total and subscale scores.

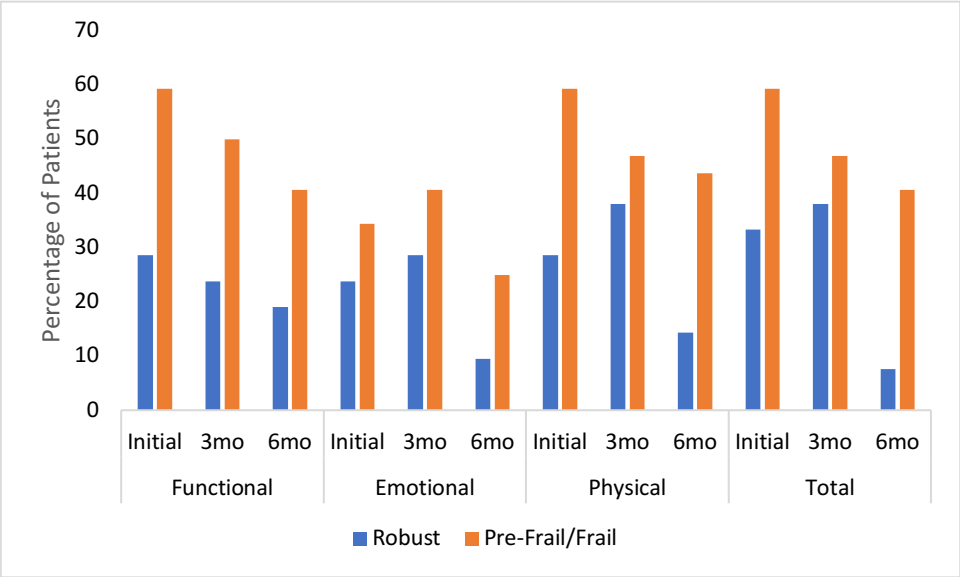
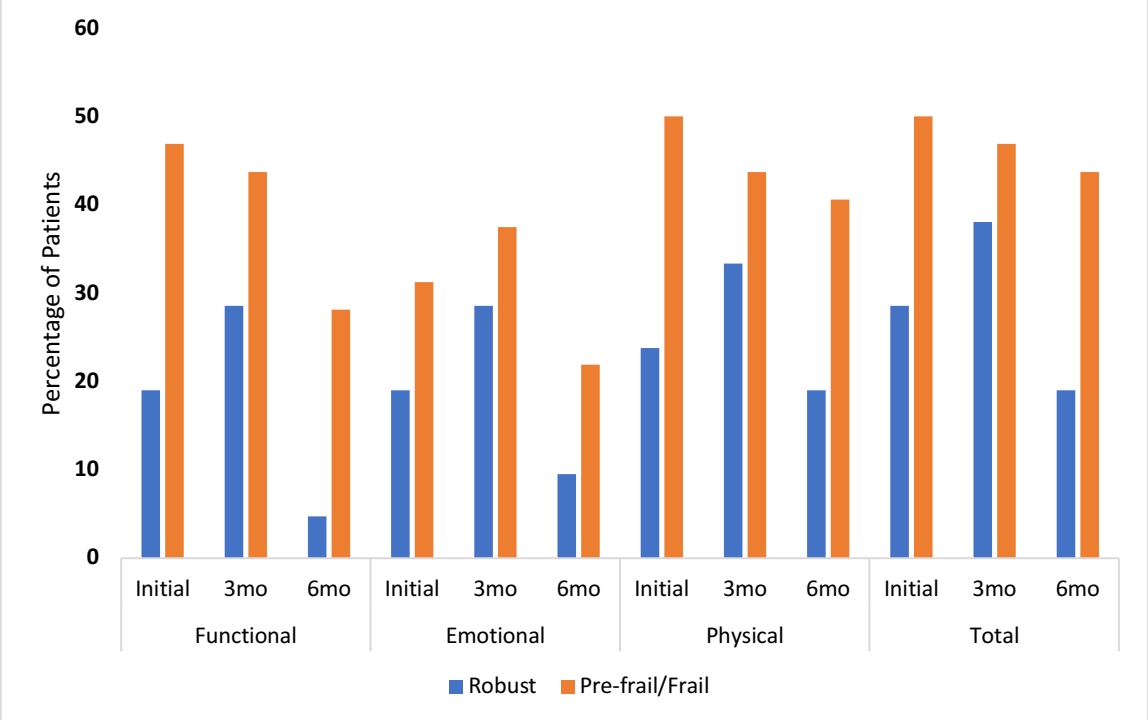


Figure 2b. Percentage of patients reporting worse swallowing post-operatively compared to pre-operatively.



CHAPTER 4.

A Protocol For A Discrete Choice Experiment: Understanding Surgeon Preferences For Recommendations In Older Adults With Well-Differentiated Thyroid Cancer.

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ABSTRACT

Introduction Older adults with well-differentiated thyroid cancer pose unique management challenges for clinicians who must weigh the risks of surgery and anesthesia with the survival benefit gained from treating their malignancy. Prior studies have demonstrated that older adults tend to undergo less treatment for their thyroid cancer. We outline a study, which aims to understand how surgical recommendations vary based on patient characteristics, extent of disease, and surgeon characteristics.

Methods and analysis We outline a protocol for the development of a discrete choice experiment (DCE), which uses a survey design. We describe both the qualitative methods used to initially design the DCE and the pilot test conducted to refine the DCE. Regression analysis will be used to refine the results.

Ethics and dissemination This study has been approved by our Institutional Review Board.

Introduction

The population of older adults in the United States (US) is on the rise. The US Census Bureau estimates a projected 58% increase in the population aged 65 and older and an 85% increase in the population age over 85 by the year 2035(96). The incidence of thyroid cancer is also on the rise(97). While thyroidectomy remains the gold standard to treat thyroid cancer, older adults (age > 65) pose unique challenges in surgical decision-making. Management decisions must weigh the risks of surgery, which are increased in the presence of co-morbidities, against the likelihood of cancer progression, morbidity, and mortality. On one hand, the majority of thyroid cancers are small, slow growing, and low risk, which suggests a more conservative approach to treatment of thyroid cancer in older adults is reasonable(98, 99). Furthermore, some evidence suggests that the increase in thyroid cancer can be attributed to over-diagnosis due to improved and more frequent use of imaging as mortality from thyroid cancer has remained essentially stable(97, 100). On the other hand, increasing patient age has been associated with higher rates of recurrence, worse prognosis, aggressive disease

characteristics, lymph node (LN) metastasis, and increased mortality suggesting perhaps a more aggressive surgical approach should be utilized(6, 101-103). Traditionally a total thyroidectomy has been performed to treat thyroid cancer, however, the most recent guidelines set forth by the American Thyroid Association indicate that thyroid lobectomy, or only removal of half of the thyroid, is acceptable management for a low-risk thyroid cancer less than 4cm in size and also that active surveillance is acceptable for a low-risk patient with a thyroid cancer of less than 1cm in size(104). Despite, this recommendation, analysis of the SEER database from 2004-2015 of patients with well-differentiated thyroid cancer demonstrated that fewer older adults actually underwent surgery and standard of care treatment compared to their younger counterparts because it was not recommended. Older adults also had a worse survival from their thyroid cancer raising the question: does extent of surgery impact survival?

The reason for recommending different treatments to older adults may be multi-factorial. While single institution studies cite the safety of thyroidectomy in older adults, population-based studies demonstrate increased rates of complications and hospital length of stay(2, 3, 5, 6, 20). Surgeon preference, comfort, and experience may affect surgical recommendations in this patient population as well. Furthermore, universally accepted guidelines regarding assessment and management of an older adult with thyroid cancer are lacking. It remains unclear how surgeons currently assess older adults and decide upon treatment recommendations or lack thereof.

Discrete choice experiment (DCE), a type of conjoint analysis, is an ideal method to study surgeon preferences and the potential trade-offs that they are willing to make in recommending surgery for various patients(105). Here, we outline a study protocol to elicit surgeon preferences regarding treatment recommendations for older adults with thyroid cancer through use of DCE. The goal of this study is to develop a survey to understand the reasons for existence of this age-related disparity in the care of older adults with well-differentiated thyroid

cancer exists. This would allow for future studies to standardize and improve the quality of care that is provided to older adults with thyroid disease.

Methods and Analysis

Rationale for using Discrete Choice Experiment (DCE)

The DCE method is a unique quantitative technique used in health care research to elicit preferences, priorities, and individual features associated with particular services. While these methods have been mainly used to understand patient preferences, they have also been applied to study clinician or surgical decision-making (106-109). DCE presents various clinical scenarios and forces respondents to make trade-offs among different treatment options, providing in depth insight into the relative importance of each characteristic, or attribute, that makes up that particular scenario. For example, a clinical scenario may be composed with three attributes such as age, functional status, and number of co-morbidities. The range of values that can describe an attribute are known as levels. Levels of a particular attribute dictate the degree of severity or how extreme a particular attribute is. For example, a clinical scenario presenting a patient can include an attribute of co-morbidity, which can then be described by three levels as follows: $\leq$ 1, 2-3, or $\geq$4. This enables identification of the particular level of an attribute that is acceptable for a provider and what trade-offs they are willing to make in recommending a procedure. DCE is an ideal approach to elicit surgeon preference for extent of procedure or lack thereof in an older adult with thyroid cancer. This methodology can delineate trade-offs that surgeons are willing to make based on various patient characteristics.

Determination of Attributes and levels

The objective of DCE is to elicit surgical preferences considering a range of attributes that define a clinical scenario. A thorough iterative process of formative research involving literature review and qualitative methods including input from various clinicians was used to generate the final list of attributes included in this DCE. First a literature review was conducted to identify possible factors that influence surgeon preferences in recommending a particular

procedure and to understand how surgeons assess older adults. A comprehensive list of factors influencing surgical recommendations was then generated (Table 1). Factors influencing extent of surgery was also obtained from case discussions at a local monthly multi-disciplinary thyroid tumor board at our institution. Members of this tumor board include endocrinologists, pathologists, radiologists, a radiation oncologist, endocrine surgeons, and otolaryngologists. Next, in-depth interviews were conducted with two endocrine surgeons and one otolaryngologist from high-volume endocrine surgery centers at two different institutions to understand what factors they use to assess an older adult's ability to tolerate surgery in addition to factors they consider for determining the extent of a procedure. The list created from the literature search was used as a platform to initiate discussion of the topics. These interviews were thirty-minute in-person interviews trying to understand which patient aspects each of the surgeons considered when counseling an older adult with thyroid cancer. The manner in which extent of disease would influence surgical recommendations was discussed as well. Multi-disciplinary expertise in survey design and planned statistical analysis of DCE was also obtained from Professors at the Bloomberg School of Public Health and the Center of Aging and Health.

Qualitative research methods were applied to identify common themes. An initial list of attributes was generated including the following: clinical intuition about the patient at the initial surgical visit ("the eyeball test"), chronological age, number or type of co-morbidities, estimate of functional status, estimate of life-expectancy, calculation of a co-morbidity or a frailty index, number of medications, input from other providers (cardiologist, internist, geriatrician, etc.), presentation at a tumor board, and obtaining opinions on a social media platform, such as a closed Facebook group of surgeons or a society-based message board. Subjective attributes, such as an eyeball test, estimate of life expectancy, and presentation at a tumor board or social media platform were eliminated. Attributes were then further narrowed down based on practical and objective assessment of an older adult in a surgical clinic and frequency of responses from key informant interviews. The level of each attribute was also constructed based on surgeon-

based focus groups, literature review, and clinical expertise. The staging system for thyroid cancer and the guidelines set forth by the American Thyroid Association were utilized to create levels for chronological age and extent of disease and also provided guidance on surgical procedures to choose from(104). Guidance for levels of attributes assessing older adults (age ≥ 65) was ascertained from aging literature and a co-morbidities model was created from the surgical literature (37, 110, 111).

Construction of Tasks

Tasks in DCE refer to the method in which the various attributes are presented to the respondents, which, in this case refers to the clinical scenario. Based on the attributes and levels in Table 1, 96 clinical scenarios were generated. To simplify the presentation of scenarios, partial profiles containing selected attributes were created in order to mimic a block design. First, 4 overarching clinical scenarios based on extent of disease were created (tumor size < 4cm and node negative, tumor size ≥ 4cm and node negative, tumor size < 4cm and node positive, tumor size ≥ 4cm and node positive). Within each of the four extent of disease scenarios, multiple different patients with varying levels of attributes for age, co-morbidity, and functional status were created. Thus, four separate extent of disease scenarios were developed each containing the same 24 patients with respect to other attributes (Fig 1). This would allow for the respondent to have a particular extent of disease in mind and select which surgical option they would recommend based on only patient-related factors, while holding extent of disease constant. The main goal of DCE, to precisely estimate preferences, requires an efficient and balanced design, must be weighed against the time and ability for a surgeon to complete the DCE and minimize illogical combinations. Based on expert opinions, clinical scenarios that seemed illogical and those that were not likely to provide additional information were eliminated. For example, including a patient with good functional status and only 0-1 co-morbidities who is < 55 and 55-64 seemed redundant in a patient with nodal disease and would not yield additional

information. To facilitate the efficient design, the four disease state scenarios were narrowed down to three. The final DCE consisted of three main scenarios with varying extent of disease (tumor size < 4cm and node negative, tumor size ≥ 4cm and node negative, tumor size < 4cm and node positive). Within each of the disease status scenarios, patient scenarios were also eliminated to yield clinically meaningful and distinct recommendations.

Survey Design

The final survey tool including the framing of the questions was developed with the assistance and review of the key informants from above. The survey instrument began with a short introduction regarding the purpose of the study. It was then divided into three sections: demographic and practice information, methods of assessing fitness for surgery and gradation of their relative importance, and finally clinical scenarios. Demographic and practice information allows the assessment of variation of preferences according to respondent characteristics. Practice information collected included years in practice after training, type of practice (endocrine surgery only versus mixed), on average number of thyroid procedures per year, and on average percent of patients seen that are over the age of 65. Key informants then reviewed the questionnaire to check for clinical accuracy and applicability. The Qualtrics XM (Provo, UT) survey interface was used to design and administer the survey tool. This survey interface was chosen due to its intuitive and easy to use user interface. Respondents had the option to not answer a question if they wished.

Pilot Testing

Pilot testing was conducted with 15 surgeons of varying backgrounds to test the face validity of the survey. Feedback was used to refine the final levels for the attributes. Specifically, the clinical scenario incorporating tumor size was modified to be greater than 4cm as respondents felt that 4cm was a gray zone that could be interpreted in different ways. Survey

flow, font size, and skip patterns on the Qualtrics interface were also modified based on verbal feedback from the pilot testing. Most participants felt that the questionnaire was clear and easy to interpret. Under the question ascertaining how surgeons assess older adults, a few were unclear on the meaning of eyeball test and therefore that answer choice was modified to include a description "overall clinical intuition about the patient when you first meet them." Pilot testing was also utilized to obtain feedback on the ease of completing the survey, feasibility, and the time taken to complete the survey. The time required to complete the survey ranged from 7 minutes to 12 minutes. All participants expressed that the scenario questions were easy to complete, though time consuming.

PROPOSED STUDY

Participant recruitment and Sampling Strategy

A lack of consensus exists regarding an adequate sample size required for DCE. A review of 69 health care-related DCE studies published in 2012 demonstrated that 32% had sample sizes of less than 100 respondents and the majority of studies, 41%, had sample sizes between 100 to 300 respondents(112). In a different systematic review evaluating DCE studies from 2005-2008 reported mean sample sizes of 100 to 300 respondents(113). We estimate a sample size between 100 to 300 participants for this study.

Eligibility criteria for participants in this study are: Surgeons practicing in the United States for at least one year and who are willing to participate. Two groups will be invited to participate: active and candidate members of The American Association of Endocrine Surgeons and The American Head and Neck Society, composed mostly of otolaryngologists. Approval will be provided from each society for distribution to its membership. Requests for member participation will be sent twice monthly over a two-month period via email.

Analytic Plan

Participant data from the two societies will initially be analyzed separately as their demographic characteristics may significantly differ. Respondent characteristics will be reported and differences will be assessed using a chi-squared test. For the DCE, respondents will be able to choose among several procedures. Therefore, initially a multinomial logit model (MNL) will be utilized to understand the tradeoffs between patient characteristics (age, functional status, co-morbidities) and choice of procedure in the clinical scenarios(105). The analysis of surgeons towards a procedure will facilitate investigation of not only which patient and disease factors (and levels) influence their recommendations for a procedure, but also will help to establish the importance of those factors. A multinomial logit (MNL) model will allow the examination of preference heterogeneity based on observed patient and disease characteristics rather than individual surgeon heterogeneity. We plan to utilize the MNL for primary data analysis because the aim of our study is to focus on predictable differences. We do intend to explore the data with the mixed MNL and generalized MNL models, both of which can be performed in STATA (version and reference). The benefit of the mixed MNL model is that it accounts for variation in preferences across respondents and models heterogeneity. All attributes will be modeled as categorical or binary variables, although, age may be explored as a continuous variable. To explore preferences between groups, a regression with parameters interacting with surgeon age, years of experience, and practice will be run. Tables of coefficients for the levels and covariates will be presented.

Discussion

To the best of the authors' knowledge, this is the first multi-step study to design a discrete choice experiment in assessing surgical decision-making for older adults with thyroid cancer. Our steps included literature review to identify factors utilized by surgeons to recommend treatments, key informant interviews, identification of key attributes and levels,

generation of clinical scenarios, and pilot testing. In this study, we built upon Coast and colleagues who recognized a two-step process to develop a DCE (114).

While DCE was originally utilized for health economics, it has been increasingly utilized to understand patient preferences mostly for treatments for diseases such as muscular dystrophy, lung cancer, leukemia, diabetes, and hepatitis C (115-119). It has been less frequently used to understand clinical decision-making, but most often used to understand treatment recommendations by gastroenterologists or surgeons for hepatocellular carcinoma (106, 107, 120). To our knowledge it the first time that a DCE would be constructed to understand treatment recommendations for thyroid cancer.

ISPOR, the professional society for health economics and outcomes research, created a task force to delineate key stages to develop a DCE (121). The construction of attributes and levels requires qualitative methods and mixed methods to generate a list of attributes and levels. A meta-analysis performed to evaluate consistency within published DCE's demonstrated that studies varied in number of attributes, which ranged from 3-16, however most included 6 attributes, 4 levels, and 73% presented 7-15 scenarios to each respondent (113). This is similar to our design, which used qualitative techniques to elicit factors surgeons felt were important and narrowed down the attributes and levels. However, our work generated multiple attributes, which necessitated narrowing down to several. Our approach to narrow down was theoretical and practical. For example, it would be difficult create a scenario for an attribute of an "eyeball test."

Once multiple clinical scenarios are generated, important structural issues to narrow down the scenarios, number of options in each choice set, and whether to include common levels of attributes in each choice set need to be addressed. Two broad approaches exist to constructing choice sets including theoretical and algorithmic and there is a lack of consensus as to which approach to employ (121). For our design, we employed a theoretical approach to narrow down clinical scenarios. However, we narrowed down the scenarios to greater than the

reported average. Finally, pilot testing enabled further iterative refinement in the wording of some of our scenarios to increase clarity.

There are several challenges to utilizing this design to evaluate surgical decision-making. The opinions of the key informant interviewees may not have fully captured the full breadth of factors that could be considered as relevant attributes, however, it is likely that it captured the majority in combination with a literature review. Additionally, we only captured opinions of surgeons, although in reality, multiple provider opinions are typically ascertained. The associated list of relevant attributes might include clinical scenarios where it is possible that interactions may exist among various attributes. Hypothetical scenarios are generated, which may limit the ability of the respondent to make a choice which would be the same choice if the patient was actually sitting in front of them. Finally, scenarios that were eliminated may provide additional insight to levels and attributes that are important.

In conclusion, this study utilized a framework as outlined by the IPSOR to develop a discrete choice experiment in the form of a survey. The major steps included literature review, key-informant interviews, generation of relevant attributes and levels, narrowing down clinical scenarios, and pilot testing. Our approach is novel to understand surgical decision-making in thyroid cancer and encourages the application of this approach to understand clinic decision-making for future studies.

Table 1. Comprehensive List of Factors that influence surgical recommendations in older adults with cancer

Factors
"Eyeball Test" or overall picture
Chronological Age
Decision-making capacity
Number of comorbidities
Types of comorbidities
Number of medications
Estimate of functional status
Frailty Index
NSQIP Risk Calculator
Comorbidity Index – charlson, Elixhauser
Input from other providers (cardiologist, internist, geriatrician)
Location of cancer
Nutritional status
Social support
Patient preference
Risk of post-operative complications
Risk of anesthesia
Reduced quality of life post-operatively
Survival benefit
Consensus after presentation at a tumor board
Obtain opinions on social media platform

Table 2. Final Attributes and Levels to use in DCE clinical scenarios

Attributes	Levels
Chronological Age	<55, 55-64, 65-79, ≥ 80
Frailty/Co-morbidity	Not-frail (0-1) co-morbidity Pre-frail (2-3) co-morbidities Frail (≥ 4) co-morbidities
Functional status	Good Poor
Nodal Status	Positive Negative
Tumor Size	< 4cm, ≥ 4cm

CHAPTER 5.

Understanding Surgical Decision-Making in Older Adults with Differentiated Thyroid Cancer: A Discrete Choice Experiment

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Abstract:

Background: Prior studies demonstrate that older adults tend to undergo less surgery for thyroid cancer. Our objective was to utilize a discrete choice experiment to identify factors influencing surgical decision-making for older adults with thyroid cancer.

Methods: Active and candidate members of the American Association of Endocrine Surgeons were invited to participate in a web-based survey. Multinomial logistic regression (MNL) was utilized to assess patient and surgeon factors associated with treatment choices.

Results: Complete survey response rate was 25.7%. Most respondents were high volume surgeons (88.5%) at academic centers (76.9%). MNL demonstrated that patient age was the strongest predictor of management. Increasing age and comorbidities were associated with the choice for active surveillance (P=0.000), not performing a lymphadenectomy in patients with nodal metastases (RRR:2.5,95%CI:1.4-4.2,P=0.002 and RRR:1.6,95%CI:1.2-2.1,P=0.004, respectively) and recommending hemithyroidectomy versus total thyroidectomy for a cancer>4cm (RRR:4.4, 95%CI:2.5-7.9,P=0.000 and RRR:3.4,95%CI:2.3-5.1,P=0.000, respectively). Surgeons with≥10 years of experience (RRR:3.3,95%CI:1.1-10.3,P=0.039) favored total thyroidectomy for a cancer<4cm, and non-fellowship trained surgeons (RRR:7.3,95%CI:1.3-42.2,P=0.027) opted for thyroidectomy without lymphadenectomy for lateral neck nodal metastases.

Conclusions: This study highlights the variation in surgical management of older adults with thyroid cancer and demonstrates the influence of patient age, comorbidities, surgeon experience, and fellowship training on management of this population.

Introduction:

The population of older adults in the U.S. is on the rise, with an estimated 58% increase in the population aged 65 and older and an 85% increase in the population aged over 85 by the year 2035(96). The incidence of thyroid cancer is also increasing across all age groups(97). While thyroidectomy remains the gold standard treatment of thyroid cancer, several population-based studies suggest that an age-related treatment variation may exist. Analysis of patients with differentiated thyroid cancer (DTC) in the Surveillance, Epidemiology, and End Results (SEER) database from 2004-2015 demonstrated that compared to younger adults, older adults (age ≥65) were more likely to undergo active surveillance and had a significantly worse disease-specific survival. Ho, et al. also found that while active surveillance may be an appropriate and safe option for younger adults with DTC, it was associated with significantly worse disease-specific survival for patients >72 years old(122). Additionally, both of these studies found that older adults underwent thyroid lobectomy more frequently compared to the younger cohort(123). While these studies demonstrate varying patterns of surgical practice, they do not adequately address the decision-making process that led to these findings.

Older adults pose unique challenges for surgical decision-making, as physicians must weigh the risks of surgery against the likelihood of cancer progression, morbidity, and mortality. On one hand, the majority of thyroid cancers are small, slow-growing, and low-risk, and despite its increasing incidence, mortality from thyroid cancer has remained stable(97, 98). Furthermore, recent studies have found that patients pursuing active surveillance for DTC ≤1.5cm have slow or minimal progression of disease, especially in older adults(124, 125). On the other hand, other studies have found that increasing patient age has been associated with higher rates of recurrence, worse prognosis, aggressive disease characteristics, lymph node (LN) metastasis, and increased mortality(6, 101, 102). While single institution studies cite the safety of thyroidectomy in older adults, population-based studies demonstrate an increased rate of complications and hospital length of stay compared to younger adults(5, 6, 20). Surgeon

preference and experience may also affect surgical recommendations in this patient population. It remains unclear how surgeons currently assess older adults and decide upon surgical treatment or lack thereof.

We therefore developed a survey, in the form of a discrete choice experiment (DCE) to understand surgeon preferences for treatment of thyroid cancer in older adults based on patient age, functional status, comorbidities, tumor size, and lymph node metastases(105). The primary objective of our study was to identify the patient and surgeon characteristics that are most influential in surgical decision-making for older patients with differentiated thyroid cancer.

Methods and Analysis:

Survey Design

The Discrete Choice Experiment (DCE) method is a unique quantitative technique used in health care research to elicit preferences, priorities, and individual features associated with particular services. While these methods have been primarily used to understand patient preferences, they have also been applied to study clinical decision-making(106, 109). DCE presents clinical scenarios and forces respondents to make trade-offs among different treatment options, providing insight into the relative importance of each characteristic, or attribute, that makes up that particular scenario. The range of values that define an attribute are known as levels.

Standard DCE methodology was used to design, implement, and analyze this survey(106). After a literature review and key informant interviews with high-volume endocrine surgeons and otolaryngologists, attributes, or characteristics, for the clinical scenarios were chosen (Table 1). Attributes included age, comorbidities, functional status, tumor size, and lateral neck lymph node status. Three overarching clinical scenarios based on extent of disease were created: 1) tumor size <4cm, node negative, 2) tumor size <4cm with lateral neck lymph node metastasis, and 3) tumor size ≥4cm, node negative. Tumor size was included to assess variation in extent of thyroidectomy (hemithyroidectomy versus total thyroidectomy), and

presence of lateral neck lymph node metastasis was utilized to assess whether a lateral neck lymph node dissection would be performed. Within each of the three extent of disease scenarios, eight patients with varying levels of attributes for age, comorbidities, and functional status were created for a total of 24 clinical scenarios (Figure 1).

In addition to the clinical scenarios, the survey instrument included questions regarding surgeon demographics and clinical practice. The survey instrument also included a question asking surgeons to select as many options from a list of various methods that they utilized to assess younger (<65 years) and older (≥65) adults' ability to tolerate surgery. This list was generated from a literature search and key informant interviews to come up with a list of attributes to include in the clinical scenarios. The respondents also chose how important they felt that the options they selected were. The survey instrument was extensively piloted to test face validity and was iteratively refined.

Under IRB approval, survey invitations were electronically distributed using the Qualtrics XM (SAP, WA, USA) interface to all candidate and active members of the American Association of Endocrine Surgeons (AAES) who practice in the United States (n= 404). The link to the survey was e-mailed with an introduction regarding its purpose and informed consent, followed by three separate reminder e-mails sent 1 week apart.

Statistical Analysis

All statistical analyses were performed using STATA version 15 (StataCorp., TX, USA). Descriptive statistics were compared using Fisher's exact test or rank sum, as appropriate. Patient scenario attributes were modeled as categorical variables. Five surgeon factors were evaluated including surgeon age, annual thyroid surgery volume (low and high volume were defined as <25 and ≥25 thyroidectomies, respectively(126)), fellowship training, years in practice, and practice limited to endocrine surgery only.

The association among the treatment choice and patient or surgeon factors for each clinical scenario was analyzed using multinomial logistic regression (MNL) with robust variance

estimates, clustered by respondent to account for within-respondent variation. Effects coding was utilized to structure the data (127). The regression provided relative prevalence ratios, which reflect the probability of choosing a particular treatment.

Results:

Respondent Characteristics

Overall survey response rate was 128/404 (31.7%), with 104 (25.7%) members completing all portions of the survey (Table 2). Of the 104 that completed the survey, the mean age was 46 years old (range 32-71). The majority of the respondents were male (56.7%), white (75%), fellowship-trained (83.6%) and high volume thyroid surgeons (88.5%). The median number of years in practice was 10 (IQR 5-18.5 years), and 46.2% reported an endocrine surgery only practice. The majority of respondents described their practice setting as academic with teaching (76.9%), followed by community hospital with an academic affiliation (17.3%), and community hospital without teaching (5.8%). Over half (56.3%) reported that 25-50% of the thyroid operations they performed in the past two years were on patients ≥65 years old.

Self-Reported Methods to Assess Older Adults

When presented with a list of options, surgeons were asked to select methods they used and felt were important to evaluate a patient's ability to tolerate surgery by age group (<65 years compared to ≥65 years) (Figure 2). Respondents placed most importance on number and type of comorbidities for patients both <65 years of age (92.9%) and ≥65 years (96.1%). For patients ≥65 years old, subjective assessment of functional status (89.2%), and the "eyeball test" or a clinician's initial intuition of the patient's health (83.3%), were the next most important methods utilized. For patients <65 years old, the frequency of use of the "eyeball test" (80.6%) was similar, but estimate of functional status (64.1%) was less commonly used for this age group.

The least important methods across all age groups were objective measures of comorbidity and functional status, with only 1.0% of respondents using a comorbidity index, and 3.9% and 7.8% of participants reported the calculation of a frailty index for patients <65 and ≥65

years of age, respectively. Chronological age was considered important by 25.2%, 35.7%, and 64.3% in patients <65, 65-79, and ≥80 years old, respectively. Other methods of assessment frequently utilized were the assessment of patient comorbidities by other physicians and an estimate of life expectancy, with the majority (75.0%) of participants saying that life expectancy <3 years would be an indication to not operate. Of the respondents, 69.5% acknowledged the existence of guidelines from the American College of Surgeons Coalition on Geriatric Surgery for the peri-operative management of older adults, but only 24.4% reported using them(128).

Association Between Treatment Decisions, Patient Factors, and Surgeon Characteristics

When presented with three overarching clinical scenarios, MNL demonstrated that age was the strongest predictor of management followed by comorbidities regardless of the tumor size or extent of disease. Poor functional status was significant in univariable MNL, but was omitted in multivariable MNL analysis due to collinearity with co-morbidities.

For the first clinical scenario, a 2.5-cm, node-negative PTC confined to the thyroid gland, significant practice variation existed. In a 40-year-old, relatively healthy patient, who served as a reference patient, 64.6% of respondents chose to perform a total thyroidectomy, 35.4% thyroid lobectomy, and none opted for active surveillance, whereas for an 88-year-old patient with ≥2 comorbidities, 11.5% chose total thyroidectomy, 17.3% thyroid lobectomy, and 71.2% active surveillance. However, 16.3% of respondents chose the same treatment for all patients in this scenario regardless of patient presentation, of which most chose hemithyroidectomy. MNL demonstrated that patient age (RRR: $3.2x10^5$, 95% CI: $2.2x10^5$-$4.5x10^5$, P= 0.000) and comorbidities (RRR: 5.8, 95% CI: 4.3-7.9, P= 0.000) were significant independent predictors for pursuing active surveillance compared to hemithyroidectomy. When comparing the choice for total versus hemithyroidectomy, patient age ≥65 was associated with a lower likelihood of recommending a total thyroidectomy (RRR: 0.7, 95% CI: 0.4-1.0, P= 0.041), whereas surgeon experience ≥10 years was associated with a higher likelihood (RRR: 3.3, 95% CI: 1.1-10.3, P= 0.039) (Table 3A).

For the second clinical scenario, a 2.5-cm PTC confined to the thyroid gland with lateral neck lymph node metastases, significant practice variation was again observed. For the reference 40- year-old patient, 88.1% of respondents chose to perform a total thyroidectomy with central and lateral neck lymph node dissection (LND), 5.9% hemithyroidectomy with central and lateral LND, 6.0% hemi- or total thyroidectomy without lateral neck LND, and 0% opted for active surveillance, whereas for an 88-year-old patient with ≥2 comorbidities, 27.7% chose to perform a total thyroidectomy with central and lateral neck LND, 7.9% hemithyroidectomy with central and lateral neck LND, 10.0% hemi- or total thyroidectomy without lateral neck LND, and 54.5% opted for active surveillance. Interestingly, 26.7% of respondents chose to perform a total thyroidectomy with central and lateral neck LND for all patients in this scenario. When comparing the choice for active surveillance to total thyroidectomy with central and lateral LND, MNL demonstrated that increasing patient age (RRR: $8.9x10^5$, 95% CI: $5.9x10^5$-$1.5x10^6$, P= 0.000) and ≥ 2 comorbidities (RRR: 9.9, 95% CI: 6.6-14.9, P= 0.000) was associated with a higher likelihood of active surveillance. Surgical practice dedicated to endocrine surgery only was associated with a lower likelihood of pursuing active surveillance (RRR: 0.4, 95% CI: 0.2-0.9; P= 0.037). Regarding management of the lateral neck lymph node metastases, factors associated with surgical management without a lateral neck LND included patient age (RRR:2.5, 95% CI: 1.4-4.7, P= 0.002) and comorbidities (RRR:1.6, 95% CI: 1.2-2.1, P= 0.004). Non-fellowship trained surgeons were also more likely to forgo lateral neck LND (RRR: 7.3, 95% CI: 1.3-42.2 P= 0.027), as were high volume surgeons (RRR: $1.6x10^7$, 95% CI: $6.7x10^6$ - $3.8x10^7$, P= 0.000) (Table 3B).

For the third clinical scenario, a 4.1-cm, node-negative PTC confined to the thyroid gland**,** variation in treatment choice was seen across age groups. In the 40-year-old reference patient, 92.1% of respondents chose to perform a total thyroidectomy, 40.6% with prophylactic central LND, 8.0% chose hemithyroidectomy, 5.0% with prophylactic central LND, and 0% opted for active surveillance, compared to an 88-year-old patient with ≥2 comorbidities, 35.7% opted

for a total thyroidectomy, 11.9% with prophylactic central LND, 25.7% chose hemithyroidectomy, 6.9% with prophylactic central LND, and 38.6% opted for active surveillance. However, 24.8% of respondents chose the same treatment for all patients, of which, 88.8% chose a total thyroidectomy, with 40.7% choosing concomitant central LND. In comparing the choice of hemithyroidectomy to total thyroidectomy, multivariable MNL demonstrated that patient age (RRR: 4.4, 95% CI: 2.5-7.9, P= 0.000) and comorbidities (RRR: 3.4, 95% CI: 2.3-5.1, P= 0.000) were significant predictors. Choice for active surveillance was also more likely with increasing patient age (RRR: $4.1x10^5$, 95% CI: $2.7x10^5$- $6.3x10^5$, P= 0.000) and comorbidities (RRR: 24.5, 95% CI:10.4-57.8, P= 0.000) (Table 3C).

Discussion:

This is the first study to utilize the discrete choice experiment (DCE) methodology to quantify the impact of key clinical and surgeon factors on the choice of therapy for older adults with thyroid cancer and to shed light on reasons for the existence of practice variation. Increasing patient age, followed by number of comorbidities, was the strongest predictor of management of thyroid cancer in older adults, and increased the likelihood of active surveillance across all scenarios. Extent of surgery was also associated with surgeon characteristics including ≥10 years of experience, surgical volume, fellowship training, and amount of practice dedicated to endocrine surgery. Finally, the preferences elicited from the scenarios identified factors deemed important for surgical decision-making, which differed from surgeon-reported factors.

Variation in choice for treatment of thyroid cancer has been well-documented and reflected in the clinical practice guidelines by the American Thyroid Association (ATA)(104, 129). Even though the majority of the participants in our study were high volume, fellowship-trained endocrine surgeons practicing at academic institutions with at least 10 years of experience, significant practice variation existed in the choice of treatment for thyroid cancer, especially regarding extent of surgery. Factors that influenced extent of thyroidectomy included

tumor size, presence of nodal metastases, patient age and comorbidities, in addition to surgeon characteristics. Surgeon experience ≥10 years was associated with a 3.3-fold higher likelihood in a tumor <4cm. Although many recent studies support the safety and adequacy of treatment with lobectomy for DTC(6, 130, 131), other studies demonstrate a high incidence of multifocality and completion lobectomies(132, 133). This inconsistency in the literature may be reflected in our results.

Factors associated with the choice for active surveillance included increasing patient age and comorbidities across all patient scenarios. There is growing evidence supporting active surveillance for PTC <1.5cm, with some studies additionally citing a lower risk of growth with increasing age(124, 125, 134). However, a recent SEER-based study by Ho, et al. showed that disease-specific mortality significantly worsened with patient age >72 years, and also for patients with tumors measuring ≥2cm that were not resected(122). Furthermore, although lymph node metastases have been associated with higher rates of recurrence and worse disease-specific survival(104), patient age and comorbidities were associated with opting for non-surgical management in patients with lateral neck lymph node involvement. It is not known if there is a patient life expectancy or other objective measure that corresponds with a survival benefit from surgery. This was exhibited in the wide range of answers reported when asked what duration of life expectancy would cause respondents to not recommend surgery. Treatment variation is not inherently a negative finding, and variation is expected in the setting of ongoing research supporting the safety of more conservative treatment strategies in select cases. However, it is important to understand the patient and surgeon factors that lead to deviation from evidence-based practice, as nonadherence to guidelines has been shown to compromise survival(135).

Not only does the DCE highlight factors important in decision-making, but this method has also been proven to determine preferences better than physician self-reflection alone(106). Respondents ranked subjective assessment of comorbidities and functional status as the most

important methods to assess surgical fitness, yet objective measurements of these factors, comorbidity and frailty indices, respectively, were used the least frequently. Additionally, less than half reported that chronological age was essential in this decision, despite the influence of age demonstrated by MNL. The subjective and wide range of pre-operative assessments coupled with treatment variation suggests that incorporating objective assessments specific to older adults with thyroid cancer may help to standardize care.

While surgical decision-making is ultimately a discussion between the patient and surgeon, the implementation of an objective surgical risk assessment tool would help to facilitate informed shared decisions without subjective biases. Extension of discrete choice experiment surveys to other physicians involved in the care of older adults with thyroid cancer, such as a broader group of surgeons and endocrinologists, would aid in further characterization of the treatment variation seen in large, population-based studies. This would then yield a platform for possible intervention.

There are several limitations of this study. First, stated preferences for choice of therapy in thyroid cancer was assessed in an idealized context as opposed to understanding actual practice patterns. Real-world scenarios would additionally include information regarding referral information, details of past medical history, unique imaging findings, or patient/family desires, which alter surgical decision-making. Referring physicians also play a significant role and may impact the choice of therapy. The response rate for completion of the survey was 25.7% for a total of 104 respondents, which is low but consistent with other DCE surveys, and non-response bias may have influenced our results(105, 106). Furthermore, all participants were endocrine surgeons, mostly general surgery-trained, and the majority had high volume practices in an academic setting with greater than 10 years of experience, which may limit the generalizability of these results as the majority of thyroid surgery is performed by low volume surgeons(126).

In conclusion, this study highlights the variation in treatment patterns for older adults with DTC and the impact of chronological age on the surgical decision-making process. While most

survey respondents did not perceive chronological age as an important factor for surgical decision-making, MNL analysis found that patient age is the most significant predictor of treatment choices, followed by patient comorbidities, while holding tumor size and extent of disease constant. Surgeon characteristics such as fellowship training, surgical volume, and years of experience also influenced the surgical recommendations delivered. Greater than 10 years of surgical experience and fellowship training were associated with a higher likelihood of performing greater extent of surgery in a patient with lateral neck lymph node metastases. As clinical practice guidelines for DTC continue to evolve, it is important to understand the factors that affect adherence to or deviation from recommended therapies in order to standardize consistent, high-quality treatment. This work encourages the incorporation of risk indices dedicated to the treatment of older adults with thyroid cancer, as well as guidelines specific to this population to optimize treatment strategies and outcomes.

Table 1. Attributes and Levels in Discrete Choice Experiment Clinical Scenarios

Attributes	Levels
Chronological Age	<55 55-64 65-79 ≥80
Comorbidities	≤1 Comorbidity 2-3 Comorbidities ≥4 Comorbidities
Functional Status	Good Poor
Nodal Status	Positive Negative
Tumor Size	<4cm ≥4cm

Table 2. Demographics and Practice Characteristics of Complete Survey Respondents

Characteristic	(n = 104) Number (%)
Mean Age (Range)	46 (32-71)
Gender	
Male	59 (56.7)
Fellowship Training	
Endocrine Surgery	70 (67.3)
Surgical Oncology	14 (13.5)
Endocrine Surgery and Surgical Oncology	1 (1.0)
Otolaryngology, Head and Neck	2 (1.9)
None	17 (16.3)
Percentage of Practice Limited to Endocrine Surgery	
100%	48 (46.2)
≥50%	32 (30.8)
≥25% but <50%	17 (16.3)
<25%	7 (6.7)
Years in Practice	
<5	23 (22.1)
5-9	28 (26.9)
10-19	28 (26.9)
≥20	25 (24.0)
Annual Volume of Thyroid Surgeries	
High (>25)	92 (88.5)
Practice Setting	
Academic with Teaching	80 (76.9)
Community with Academic Affiliation	18 (17.3)
Community	6 (5.8)

Table 3A. Node Negative PTC <4cm: Patient and Surgical Determinants of Choice for Total Thyroidectomy or Active Surveillance Compared to Thyroid Lobectomy.

Characteristic	Total Thyroidectomy vs. Thyroid Lobectomy (Ref)			Active Surveillance vs. Thyroid Lobectomy (Ref)		
	RRR	95% CI	P Value	RRR	95% CI	P value
Patient Attributes						
Age						
<55 Years	Ref			Ref		
55-64 Years	1.1	0.9-1.3	0.35	27.4*	19.9-37.5	0.000
Age ≥65	0.7*	0.4-1.0	0.041	$1.2x10^{4}$*	$8.0x10^{3}$-$1.7x10^{4}$	0.000
65-79 Years	1.0	0.8-1.2	0.92	39.0*	30.3-50.2	0.000
≥80 Years	0.6*	0.4-0.9	0.03	296.2*	222.8-393.8	0.000
Comorbidities						
≤ 1	Ref			Ref		
≥2 Comorbidities	0.9	0.7-1.1	0.286	5.8*	4.3-7.9	0.000
2-3	0.9	0.7-1.1	0.375	1.8*	1.4-2.3	0.000
≥4	0.9	0.7-1.2	0.626	3.6*	2.6-5.0	0.000
Surgeon Characteristics						
Age	1.0	0.9-1.0	0.179	1.0	0.9-1.0	0.365
Years in Practice						
< 10	Ref			Ref		
≥10	3.3*	1.1-10.3	0.039	2.4	0.9-5.6	0.079
Fellowship Training						
Yes	Ref			Ref		
No	1.5	0.5-4.8	0.462	0.5	0.2-1.3	0.140
Endocrine Surgery Only Practice						
Yes	Ref			Ref		
No	1.3	0.6-2.7	0.513	0.8	0.4-1.5	0.421
Annual Volume						
Low	Ref			Ref		
High	0.3	0.04-1.5	0.131	0.9	0.3-2.3	0.746

Ref= Reference
RRR= Relative Risk Ratio
CI= Confidence Interval
Functional status omitted due to co-linearity with co-morbidities
*All P values set for significance <0.05

Table 3B. Node Positive PTC <4cm: Patient and Surgical Determinants of Choice for Management of Lateral Neck Lymph Node Metastasis and Choice for Active Surveillance compared to Total Thyroidectomy with Central & Lateral Neck Dissection.

Characteristic	-Lymphadenectomy vs. +Lymphadenectomy (Ref)			Active Surveillance vs. Total Thyroidectomy with Central & Lateral Neck Dissection (Ref)		
	RRR	95% CI	P value	RRR	95% CI	P value
Patient Attributes						
Age						
<55 Years	Ref			Ref		
55-64 Years	1.0	0.8-1.2	0.991	29.3*	20.9-41.2	0.000
Age ≥65	2.5*	1.5-4.4	0.001	$3.0x10^4$*	$2.1x10^4$-$4.5x10^4$	0.000
65-79 Years	1.2	0.9-1.5	0.144	72.7*	56.9-92.9	0.000
≥80 Years	2.1*	1.4-3.3	0.000	419.1*	299.8-585.9	0.000
Comorbidities						
0-1	Ref			Ref		
≥2 Comorbidities	1.6*	1.2-2.1	0.004	9.9*	6.6-14.9	0.000
2-3	1.2	0.9-1.6	0.264	2.9*	2.1-4.1	0.000
≥4	1.3	1.0-1.9	0.093	3.4*	2.5-4.7	0.000
Surgeon Characteristics						
Age	1.0	0.9-1.1	0.866	1.0	0.9-1.0	0.386
Years in Practice						
<10	Ref			Ref		
≥10	0.3	0.1-1.8	0.195	3.0	1.0-9.0	0.052
Fellowship Training						
Yes	Ref			Ref		
No	7.3*	1.3-42.2	0.027	0.7	0.2-2.1	0.489
Endocrine Surgery Only Practice						
Yes	Ref			Ref		
No	0.3	0.1-1.0	0.053	0.4*	0.2-0.9	0.037
Annual Volume						
Low	Ref			Ref		
High	$1.6x10^7$*	$6.7x10^6$-$3.8x10^7$	0.000	1.4	0.3-6.5	0.634

Ref= Reference
RRR= Relative Risk Ratio
CI= Confidence Interval
Functional status omitted due to co-linearity with co-morbidities
*All P values set for significance <0.05

Table 3C. Node Negative PTC >4 cm: Patient and Surgical Determinants of Choice for Thyroid Lobectomy or Active Surveillance Compared to Total Thyroidectomy.

Characteristic	Thyroid Lobectomy vs. Total Thyroidectomy (Ref)			Active Surveillance vs. Total Thyroidectomy (Ref)		
	RRR	95% CI	P value	RRR	95% CI	P value
Patient Attributes						
Patient Age						
<55 Years	Ref			Ref		
55-64 Years	0.8	0.6-1.1	0.147	10.5*	5.6-19.9	0.000
Age ≥65	5.4*	3.1-9.7	0.000	$3.8x10^{4}$*	$2.2x10^{4}$-$6.8x10^{4}$	0.000
65-79 Years	1.2	1.0-1.6	0.090	32.8*	22.2-48.5	0.000
≥80 Years	4.3*	2.7-6.9	0.000	1191.3*	623.0-2278.3	0.000
Comorbidities						
0-1	Ref			Ref		
≥2 Comorbidities	3.4*	2.3-5.1	0.000	24.5*	10.4-57.8	0.000
2-3	1.6	1.3-1.9	0.144	4.2*	2.8-6.2	0.000
≥4	2.0*	1.6-2.7	0.000	6.7*	3.8-11.9	0.000
Surgeon Characteristics						
Age	1.0	0.9-1.1	0.884	1.0	0.9-1.1	0.882
Years in Practice						
<10	Ref			Ref		
≥10	1.0	0.3-3.3	0.961	1.7	0.5-5.5	0.407
Fellowship Training						
Yes	Ref			Ref		
No	1.4	10.5-4.3	0.535	0.8	0.2-2.7	0.683
Endocrine Surgery Only Practice						
Yes	Ref			Ref		
No	1.5	0.7-3.3	0.300	0.7	0.3-1.7	0.468
Annual Volume						
Low	Ref			Ref		
High	0.6	0.2-2.2	0.462	2.2	0.3-15.3	0.430

Ref= Reference
RRR= Relative Risk Ratio
CI= Confidence Interval
Functional status omitted due to co-linearity with co-morbidities
*All P values set for significance <0.05

Figures

Figure 1. Sample of a portion of the first clinical scenario in survey

A male presents with a 2.5 cm palpable, mobile, right-sided PTC with no compressive symptoms. No suspicious lymph nodes are seen on ultrasound. He has no family history of thyroid cancer or prior exposure to XRT. What would you recommend for each of the following patients?

	Management Options		
	Right thyroid lobectomy (1)	Total thyroidectomy (2)	Active Surveillance (3)
40 year old with diabetes, COPD, and hypertension. He lives alone and takes care of himself. (1)	○	○	○
60 year old with diabetes, COPD, and hypertension. He lives alone and takes care of himself. (2)	○	○	○

Figure 2. Surgeon-reported methods deemed important when assessing patients for surgical management of thyroid cancer

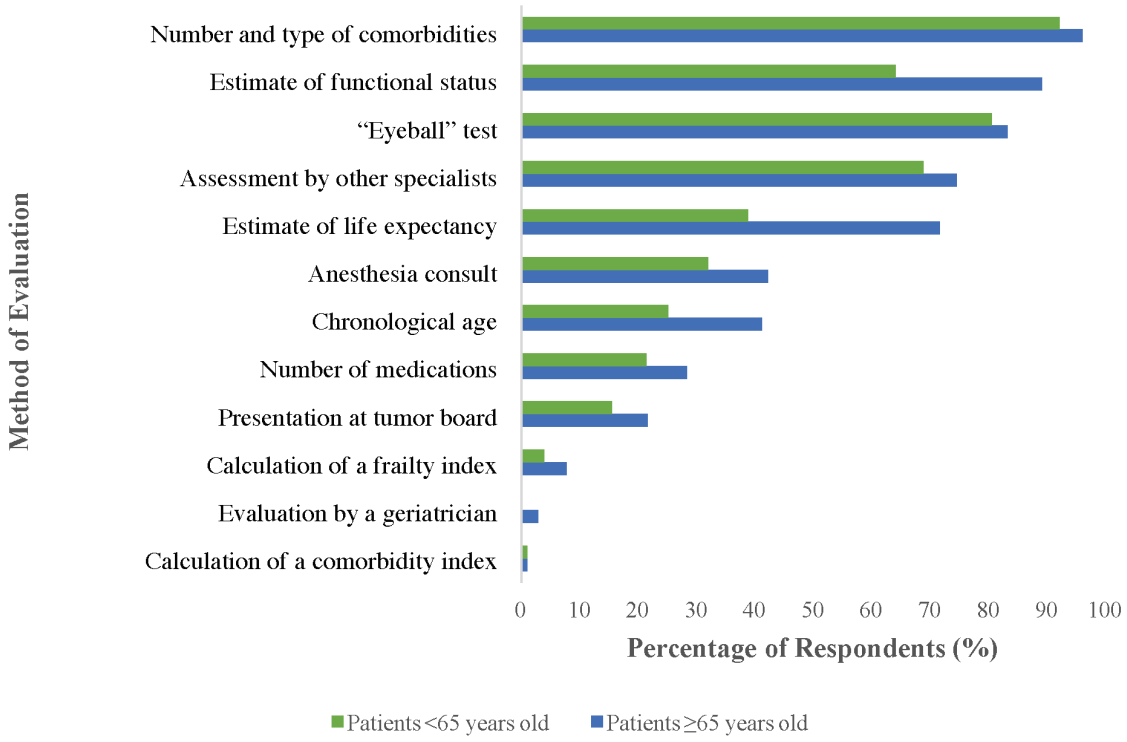
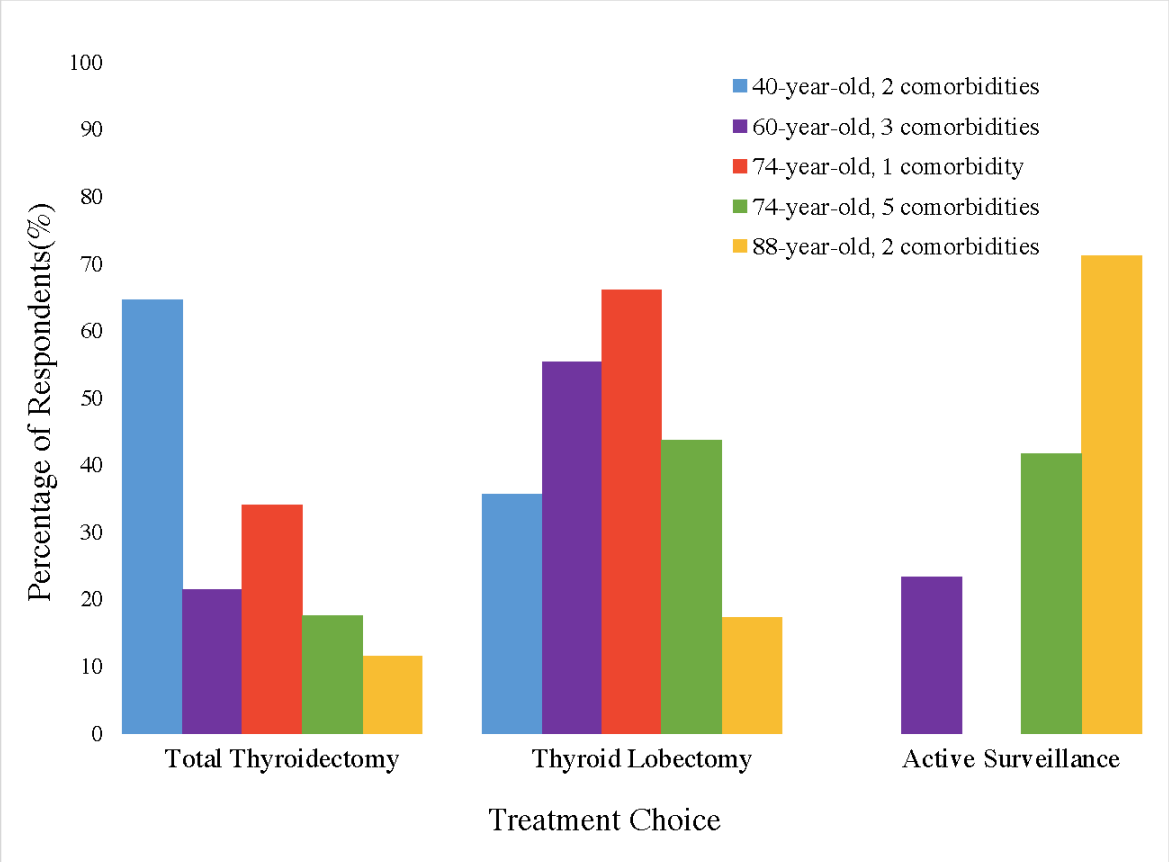


Figure 3. Treatment variation for adults with papillary thyroid cancer (PTC) in 3 overarching clinical scenarios, stratified by patient scenario.

Figure 3A. Treatment Choice for Various Patients with a 2.5cm, Node-Negative PTC



PTC: Papillary Thyroid Cancer

Figure 3B. Treatment Choice for Various Patients with a 2.5cm PTC with Lateral Neck Lymph Node Metastasis

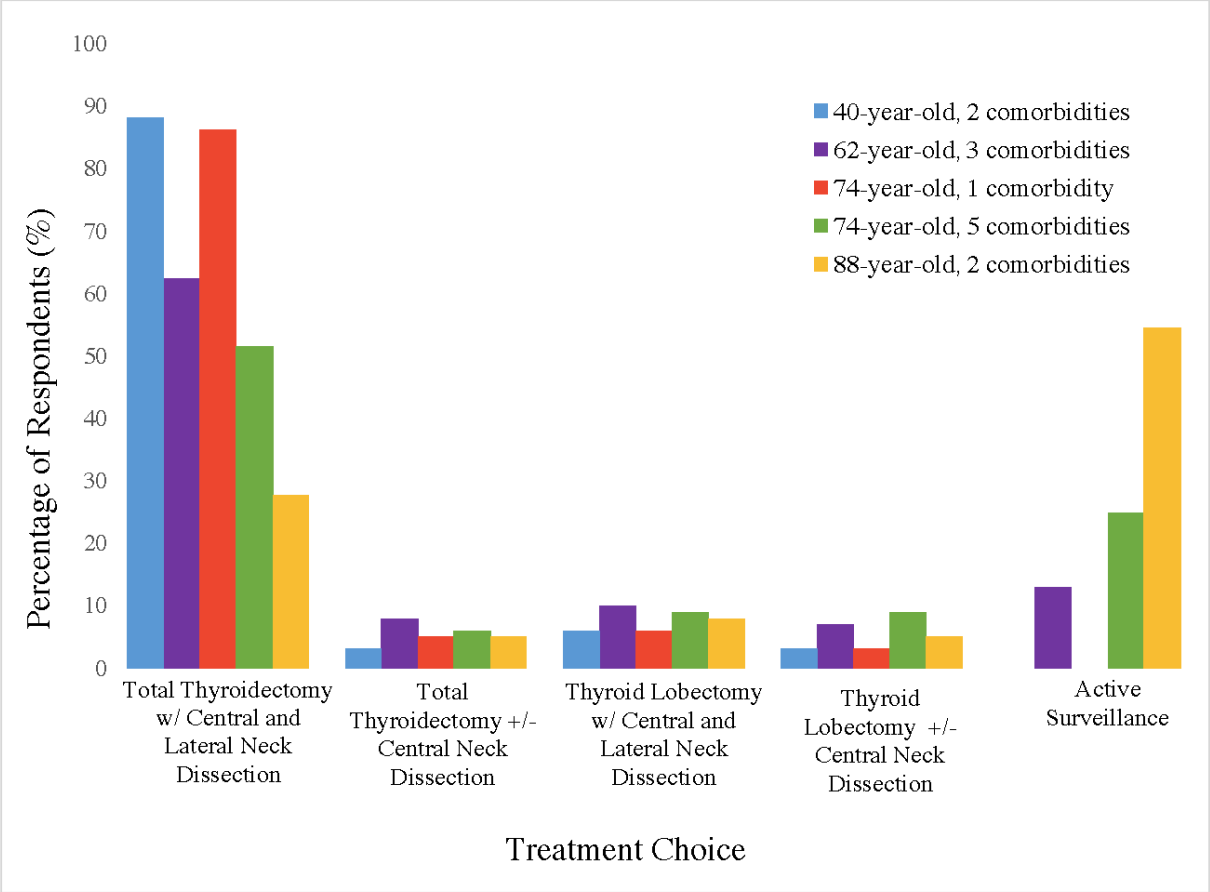
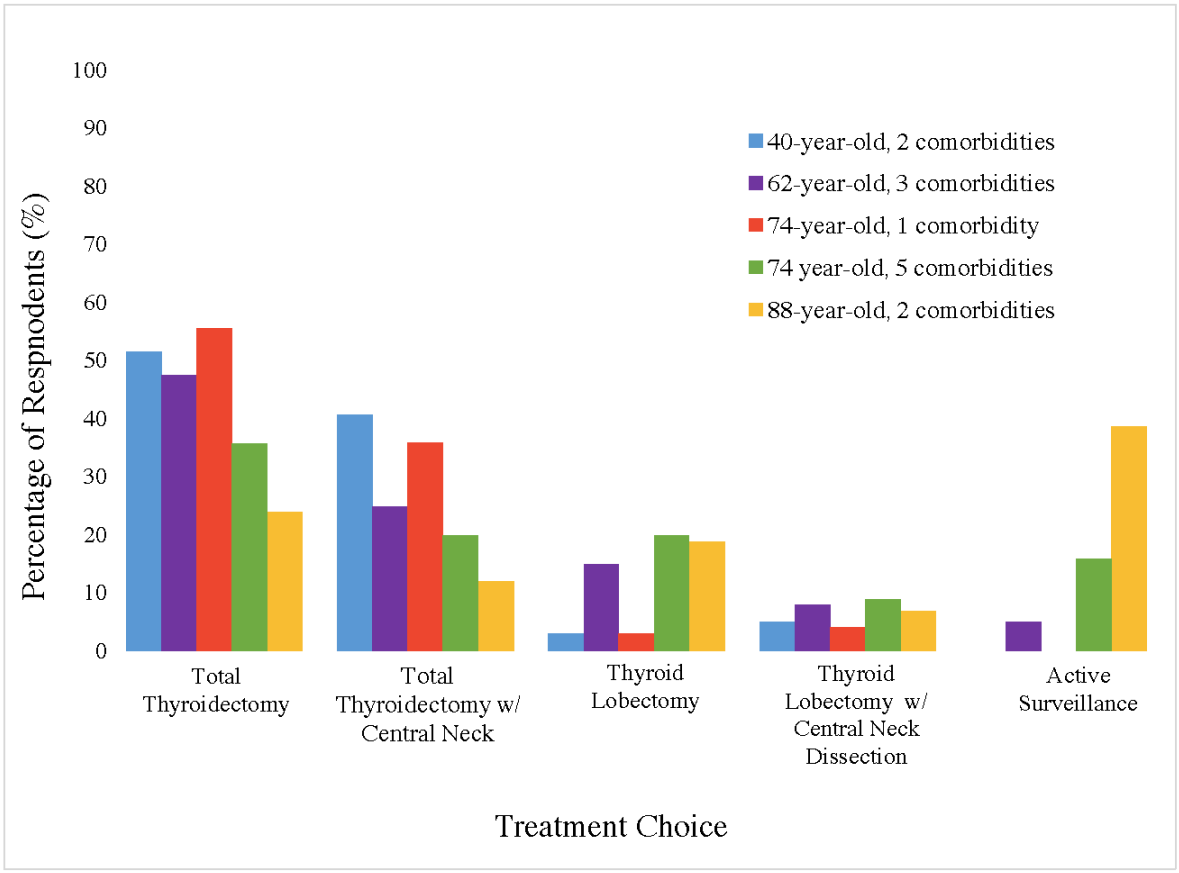


Figure 3C. Treatment Choice for Various Patients with a 4.1cm, Node-Negative PTC



CHAPTER 6.

Conclusions

From our longitudinal prospective cohort study, we found a high prevalence of voice and swallowing impairments in older patients pre-operatively as evidence by 67.9% of patients having abnormal VHI scores and 77.4% having abnormal DHI. Compared to the pre-operative time point, early post-thyroidectomy, almost half of the patients in this cohort had higher VHI scores and this persisted up to 6 months in almost 1/3 of patients. Compared to pre-operative assessment, post-thyroidectomy 41.5% of patients reported worse swallowing at the initial post-operative visit and this persisted in 32.1% at 6 months.

When evaluating risk factors for voice changes, on unadjusted analyses, frailty was associated with adverse voice and swallowing outcomes, which affected quality of life. Frailty was specifically associated with adverse outcomes in the functional and physical subscales of voice in the early post-operative period. BMI was also associated with adverse functional voice outcomes in the early post-operative period. Frailty was also associated with adverse functional dysphagia outcomes in the early post-operative period. Functional voice outcomes affect activities of daily living.

From our study of eliciting how surgeons assess older adults for surgery, the most commonly used method was the eyeball test or clinical intuition about the patient. From responses to our survey questions, multinomial logistic regression demonstrated that patient age was the strongest predictor for extent of surgery or lack thereof.

Increasing age and comorbidities were associated with the choice for active surveillance of a thyroid cancer cancer <4cm, not performing a lymphadenectomy in patients with nodal metastases, and recommending hemithyroidectomy versus total thyroidectomy for a cancer>4cm. Surgeons with≥10 years of experience favored total thyroidectomy for a cancer<4cm, and non-fellowship trained surgeons opted for thyroidectomy without lymphadenectomy for lateral neck nodal metastases.

Our final study highlights the variation in treatment patterns for older adults with DTC and the impact of chronological age on the surgical decision-making process. While most survey respondents did not perceive chronological age as an important factor for surgical decision-making, MNL analysis found that patient age is the most significant predictor of treatment choices, followed by patient comorbidities, while holding tumor size and extent of disease constant. Surgeon characteristics such as fellowship training, surgical volume, and years of experience also influenced the surgical recommendations delivered. Greater than 10 years of surgical experience and fellowship training were associated with a higher likelihood of performing greater extent of surgery in a patient with lateral neck lymph node metastases. As clinical practice guidelines for DTC continue to evolve, it is important to understand the factors that affect adherence to or deviation from recommended therapies in order to standardize consistent, high-quality treatment. This work encourages the incorporation of risk indices dedicated to the treatment of older adults with thyroid cancer, as well as guidelines specific to this population to optimize treatment strategies and outcomes.

Overall our work highlights the treatment variation in surgical recommendations, lack of consistency in evaluation of older patients in need of thyroidectomy, and suggests that frailty, a measure of physiologic age, may better reflect how well patients will tolerate surgery. Prior studies have demonstrated varying surgical recommendation for thyroid cancer (129, 136, 137). These studies have demonstrated variation in rates of hemithyroidectomy versus total thyroidectomy, the role of central neck dissection, thyroid hormone management after surgery, and radioactive iodine use. Our work is unique in that it provides insight into how surgeons place emphasis on certain factors to provide recommendations, the variation on those factors, in addition to the lack of objective measures utilized for decision-making.

Our work also highlights the need for a measure of physiologic reserve, not just to aid in decision-making, but to also assess outcomes. Voice and swallowing impairments post-thyroidectomy are infrequently related to nerve injury, however, they have a significant impact

on a patient's quality of life. Identifying patients at risk for these adverse outcomes will aid in early or even pre-operative referral to voice or swallowing rehabilitation. Significant work still needs to be done on a larger scale to assess the frailty phenotype as a measure of physiologic age to predict voice and swallowing changes after thyroidectomy especially as older patients are living longer. There is also significant work that needs to be done to convey the concept of physiologic age as opposed to chronologic age to the multitude of surgeons performing thyroidectomy procedures and the referring endocrinologists. Additionally, once at risk patients are identified, interventions should be explored that may help to mitigate these changes.

References

1. Russo A. AHRQ Healthcare Cost and Utilization Project Statistical Brief #86 2007 [2015]. Available from: www.hcup-us.ahrq.gov/reports/statbriefs/sb86.pdf.
2. Bliss R, Patel N, Guinea A, Reeve TS, Delbridge L. Age is no contraindication to thyroid surgery. Age Ageing. 1999;28(4):363-6. Epub 1999/08/25. doi: 10.1093/ageing/28.4.363. PubMed PMID: 10459789.
3. Passler C, Avanessian R, Kaczirek K, Prager G, Scheuba C, Niederle B. Thyroid surgery in the geriatric patient. Arch Surg. 2002;137(11):1243-8. Epub 2002/11/07. doi: 10.1001/archsurg.137.11.1243. PubMed PMID: 12413310.
4. Sosa JA, Mehta PJ, Wang TS, Boudourakis L, Roman SA. A population-based study of outcomes from thyroidectomy in aging Americans: at what cost? J Am Coll Surg. 2008;206(6):1097-105. Epub 2008/05/27. doi: 10.1016/j.jamcollsurg.2007.11.023. PubMed PMID: 18501806.
5. Sahli ZT, Zhou S, Najjar O, Onasanya O, Segev D, Massie A, Zeiger MA, Mathur A. Octogenarians have worse clinical outcomes after thyroidectomy. Am J Surg. 2018;216(6):1171-6. doi: 10.1016/j.amjsurg.2018.04.013. PubMed PMID: 29729944; PMCID: PMC6197934.
6. Park HS, Roman SA, Sosa JA. Treatment patterns of aging Americans with differentiated thyroid cancer. Cancer. 2010;116(1):20-30. Epub 2009/11/13. doi: 10.1002/cncr.24717. PubMed PMID: 19908255.
7. Sutton W, Canner JK, Segev DL, Zeiger MA, Mathur A. Treatment Variation in Older Adults With Differentiated Thyroid Cancer. J Surg Res. 2020;254:154-64. Epub 2020/05/24. doi: 10.1016/j.jss.2020.04.013. PubMed PMID: 32445931; PMCID: PMC7483795.
8. Grover G, Sadler GP, Mihai R. Morbidity after thyroid surgery: patient perspective. The Laryngoscope. 2013;123(9):2319-23. doi: 10.1002/lary.23850. PubMed PMID: 23824630.
9. Hong KH, Yang YS, Lee HD, Yoon YS, Hong YT. The effect of total thyroidectomy on the speech production. Clinical and experimental otorhinolaryngology. 2015;8(2):155-60. doi: 10.3342/ceo.2015.8.2.155. PubMed PMID: 26045915; PMCID: 4451541.
10. Scerrino G, Inviati A, Di Giovanni S, Paladino NC, Di Paola V, Lo Re G, Almasio PL, Cupido F, Gulotta G, Bonventre S. Esophageal motility changes after thyroidectomy; possible associations with postoperative voice and swallowing disorders: preliminary results. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery. 2013;148(6):926-32. doi: 10.1177/0194599813482299. PubMed PMID: 23525853.
11. Oren A, Benoit MA, Murphy A, Schulte F, Hamilton J. Quality of life and anxiety in adolescents with differentiated thyroid cancer. The Journal of clinical endocrinology and metabolism. 2012;97(10):E1933-7. doi: 10.1210/jc.2012-1823. PubMed PMID: 22791758.
12. Roberts KJ, Lepore SJ, Urken ML. Quality of life after thyroid cancer: an assessment of patient needs and preferences for information and support. Journal of cancer education : the official journal of the American Association for Cancer Education. 2008;23(3):186-91. doi: 10.1080/08858190802247762. PubMed PMID: 18709591.

13. Shah MD, Witterick IJ, Eski SJ, Pinto R, Freeman JL. Quality of life in patients undergoing thyroid surgery. The Journal of otolaryngology. 2006;35(4):209-15. PubMed PMID: 17176794.
14. [2016]. Available from: www.hcup-us.ahrq.gov/reports/statbriefs/sb86.pdf.
15. Mazzaferri EL. Management of a solitary thyroid nodule. The New England journal of medicine. 1993;328(8):553-9. doi: 10.1056/NEJM199302253280807. PubMed PMID: 8426623.
16. Dean DS, Gharib H. Epidemiology of thyroid nodules. Best practice & research Clinical endocrinology & metabolism. 2008;22(6):901-11. doi: 10.1016/j.beem.2008.09.019. PubMed PMID: 19041821.
17. Kitahara CM, Sosa JA. Understanding the ever-changing incidence of thyroid cancer. Nat Rev Endocrinol. 2020;16(11):617-8. Epub 2020/09/09. doi: 10.1038/s41574-020-00414-9. PubMed PMID: 32895503; PMCID: PMC7476643.
18. Older Population and Aging [cited 2021 March 10]. Available from: https://www.census.gov/topics/population/older-aging.html.
19. Mather M JL, Pollard KM. . Aging in the United States. Population Bulletin. 2015:1-18.
20. Seybt MW, Khichi S, Terris DJ. Geriatric thyroidectomy: safety of thyroid surgery in an aging population. Arch Otolaryngol Head Neck Surg. 2009;135(10):1041-4. doi: 10.1001/archoto.2009.138. PubMed PMID: 19841346.
21. Sosa JA, Mehta PJ, Wang TS, Boudourakis L, Roman SA. A population-based study of outcomes from thyroidectomy in aging Americans: at what cost? Journal of the American College of Surgeons. 2008;206(3):1097-105. doi: 10.1016/j.jamcollsurg.2007.11.023. PubMed PMID: 18501806.
22. Tuggle CT, Park LS, Roman S, Udelsman R, Sosa JA. Rehospitalization among elderly patients with thyroid cancer after thyroidectomy are prevalent and costly. Annals of surgical oncology. 2010;17(11):2816-23. doi: 10.1245/s10434-010-1144-7. PubMed PMID: 20552406.
23. Jeannon JP, Orabi AA, Bruch GA, Abdalsalam HA, Simo R. Diagnosis of recurrent laryngeal nerve palsy after thyroidectomy: a systematic review. International journal of clinical practice. 2009;63(4):624-9. doi: 10.1111/j.1742-1241.2008.01875.x. PubMed PMID: 19335706.
24. Arakawa-Sugueno L, Ferraz AR, Morandi J, Capobianco DM, Cernea CR, Sampaio MA, Kulcsar MA, Simoes CA, Brandao LG. Videoendoscopic Evaluation of Swallowing After Thyroidectomy: 7 and 60 Days. Dysphagia. 2015;30(5):496-505. doi: 10.1007/s00455-015-9628-z. PubMed PMID: 26087901.
25. Vicente DA, Solomon NP, Avital I, Henry LR, Howard RS, Helou LB, Coppit GL, Shriver CD, Buckenmaier CC, Libutti SK, Shaha AR, Stojadinovic A. Voice outcomes after total thyroidectomy, partial thyroidectomy, or non-neck surgery using a prospective multifactorial assessment. J Am Coll Surg. 2014;219(1):152-63. doi: 10.1016/j.jamcollsurg.2014.03.019. PubMed PMID: 24745621.
26. Kuhn MA. Histological changes in vocal fold growth and aging. Current opinion in otolaryngology & head and neck surgery. 2014;22(6):460-5. doi: 10.1097/MOO.0000000000000108. PubMed PMID: 25232935.
27. Rogers DJ, Setlur J, Raol N, Maurer R, Hartnick CJ. Evaluation of true vocal fold growth as a function of age. Otolaryngology--head and neck surgery : official journal of

American Academy of Otolaryngology-Head and Neck Surgery. 2014;151(4):681-6. doi: 10.1177/0194599814547489. PubMed PMID: 25171926.
28. Vaca M, Mora E, Cobeta I. The Aging Voice: Influence of Respiratory and Laryngeal Changes. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery. 2015;153(3):409-13. doi: 10.1177/0194599815592373. PubMed PMID: 26156424.
29. Martins RH, Benito Pessin AB, Nassib DJ, Branco A, Rodrigues SA, Matheus SM. Aging voice and the laryngeal muscle atrophy. The Laryngoscope. 2015. doi: 10.1002/lary.25398. PubMed PMID: 26154530.
30. Wang CM, Chen JY, Chuang CC, Tseng WC, Wong AM, Pei YC. Aging-related changes in swallowing, and in the coordination of swallowing and respiration determined by novel non-invasive measurement techniques. Geriatrics & gerontology international. 2015;15(6):736-44. doi: 10.1111/ggi.12343. PubMed PMID: 25257507.
31. Davids T, Klein AM, Johns MM, 3rd. Current dysphonia trends in patients over the age of 65: is vocal atrophy becoming more prevalent? Laryngoscope. 2012;122(2):332-5. Epub 2012/01/19. doi: 10.1002/lary.22397. PubMed PMID: 22252988.
32. de Araujo Pernambuco L, Espelt A, Balata PM, de Lima KC. Prevalence of voice disorders in the elderly: a systematic review of population-based studies. Eur Arch Otorhinolaryngol. 2015;272(10):2601-9. Epub 2014/08/26. doi: 10.1007/s00405-014-3252-7. PubMed PMID: 25149291.
33. Golub JS, Chen PH, Otto KJ, Hapner E, Johns MM, 3rd. Prevalence of perceived dysphonia in a geriatric population. J Am Geriatr Soc. 2006;54(11):1736-9. Epub 2006/11/08. doi: 10.1111/j.1532-5415.2006.00915.x. PubMed PMID: 17087701.
34. Roy N, Stemple J, Merrill RM, Thomas L. Epidemiology of voice disorders in the elderly: preliminary findings. Laryngoscope. 2007;117(4):628-33. Epub 2007/04/13. doi: 10.1097/MLG.0b013e3180306da1. PubMed PMID: 17429872.
35. Xue QL. The frailty syndrome: definition and natural history. Clin Geriatr Med. 2011;27(1):1-15. Epub 2010/11/26. doi: 10.1016/j.cger.2010.08.009. PubMed PMID: 21093718; PMCID: PMC3028599.
36. Xue QL, Bandeen-Roche K, Tian J, Kasper JD, Fried LP. Progression of Physical Frailty and the Risk of All-Cause Mortality: Is There a Point of No Return? J Am Geriatr Soc. 2021;69(4):908-15. Epub 2020/12/29. doi: 10.1111/jgs.16976. PubMed PMID: 33368158; PMCID: PMC8049969.
37. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA, Cardiovascular Health Study Collaborative Research G. Frailty in older adults: evidence for a phenotype. The journals of gerontology Series A, Biological sciences and medical sciences. 2001;56(3):M146-56. PubMed PMID: 11253156.
38. Newman AB, Gottdiener JS, McBurnie MA, Hirsch CH, Kop WJ, Tracy R, Walston JD, Fried LP, Cardiovascular Health Study Research G. Associations of subclinical cardiovascular disease with frailty. The journals of gerontology Series A, Biological sciences and medical sciences. 2001;56(3):M158-66. PubMed PMID: 11253157.
39. Folsom AR, Boland LL, Cushman M, Heckbert SR, Rosamond WD, Walston JD. Frailty and risk of venous thromboembolism in older adults. The journals of gerontology Series A, Biological sciences and medical sciences. 2007;62(1):79-82. PubMed PMID: 17301042.

40. Boyd CM, Xue QL, Simpson CF, Guralnik JM, Fried LP. Frailty, hospitalization, and progression of disability in a cohort of disabled older women. The American journal of medicine. 2005;118(11):1225-31. doi: 10.1016/j.amjmed.2005.01.062. PubMed PMID: 16271906.
41. Makary MA, Segev DL, Pronovost PJ, Syin D, Bandeen-Roche K, Patel P, Takenaga R, Devgan L, Holzmueller CG, Tian J, Fried LP. Frailty as a predictor of surgical outcomes in older patients. Journal of the American College of Surgeons. 2010;210(6):901-8. doi: 10.1016/j.jamcollsurg.2010.01.028. PubMed PMID: 20510798.
42. Garonzik-Wang JM, Govindan P, Grinnan JW, Liu M, Ali HM, Chakraborty A, Jain V, Ros RL, James NT, Kucirka LM, Hall EC, Berger JC, Montgomery RA, Desai NM, Dagher NN, Sonnenday CJ, Englesbe MJ, Makary MA, Walston JD, Segev DL. Frailty and delayed graft function in kidney transplant recipients. Arch Surg. 2012;147(2):190-3. Epub 2012/02/22. doi: 10.1001/archsurg.2011.1229. PubMed PMID: 22351919.
43. Haugen CE, Mountford A, Warsame F, Berkowitz R, Bae S, Thomas AG, Brown CHt, Brennan DC, Neufeld KJ, Carlson MC, Segev DL, McAdams-DeMarco M. Incidence, Risk Factors, and Sequelae of Post-kidney Transplant Delirium. J Am Soc Nephrol. 2018;29(6):1752-9. Epub 2018/04/25. doi: 10.1681/ASN.2018010064. PubMed PMID: 29685884; PMCID: PMC6054339.
44. McAdams-DeMarco MA, King EA, Luo X, Haugen C, DiBrito S, Shaffer A, Kucirka LM, Desai NM, Dagher NN, Lonze BE, Montgomery RA, Walston J, Segev DL. Frailty, Length of Stay, and Mortality in Kidney Transplant Recipients: A National Registry and Prospective Cohort Study. Ann Surg. 2017;266(6):1084-90. Epub 2016/09/23. doi: 10.1097/SLA.0000000000002025. PubMed PMID: 27655240; PMCID: PMC5360544.
45. McAdams-DeMarco MA, Law A, King E, Orandi B, Salter M, Gupta N, Chow E, Alachkar N, Desai N, Varadhan R, Walston J, Segev DL. Frailty and mortality in kidney transplant recipients. Am J Transplant. 2015;15(1):149-54. Epub 2014/11/02. doi: 10.1111/ajt.12992. PubMed PMID: 25359393; PMCID: PMC4332809.
46. McAdams-DeMarco MA, Law A, Salter ML, Chow E, Grams M, Walston J, Segev DL. Frailty and early hospital readmission after kidney transplantation. Am J Transplant. 2013;13(8):2091-5. Epub 2013/06/05. doi: 10.1111/ajt.12300. PubMed PMID: 23731461; PMCID: PMC4000567.
47. McAdams-DeMarco MA, Olorundare IO, Ying H, Warsame F, Haugen CE, Hall R, Garonzik-Wang JM, Desai NM, Walston JD, Norman SP, Segev DL. Frailty and Postkidney Transplant Health-Related Quality of Life. Transplantation. 2018;102(2):291-9. Epub 2017/09/09. doi: 10.1097/TP.0000000000001943. PubMed PMID: 28885489; PMCID: PMC5790611.
48. Afilalo J, Lauck S, Kim DH, Lefevre T, Piazza N, Lachapelle K, Martucci G, Lamy A, Labinaz M, Peterson MD, Arora RC, Noiseux N, Rassi A, Palacios IF, Genereux P, Lindman BR, Asgar AW, Kim CA, Trnkus A, Morais JA, Langlois Y, Rudski LG, Morin JF, Popma JJ, Webb JG, Perrault LP. Frailty in Older Adults Undergoing Aortic Valve Replacement: The FRAILTY-AVR Study. J Am Coll Cardiol. 2017;70(6):689-700. Epub 2017/07/12. doi: 10.1016/j.jacc.2017.06.024. PubMed PMID: 28693934.
49. Shi S, Afilalo J, Lipsitz LA, Popma JJ, Khabbaz KR, Laham RJ, Guibone K, Grodstein F, Lux E, Kim DH. Frailty Phenotype and Deficit Accumulation Frailty Index in Predicting Recovery After Transcatheter and Surgical Aortic Valve Replacement. J Gerontol A Biol Sci

Med Sci. 2019;74(8):1249-56. Epub 2018/08/31. doi: 10.1093/gerona/gly196. PubMed PMID: 30165422; PMCID: PMC6625585.
50. Seib CD, Rochefort H, Chomsky-Higgins K, Gosnell JE, Suh I, Shen WT, Duh QY, Finlayson E. Association of Patient Frailty With Increased Morbidity After Common Ambulatory General Surgery Operations. JAMA Surg. 2018;153(2):160-8. Epub 2017/10/20. doi: 10.1001/jamasurg.2017.4007. PubMed PMID: 29049457; PMCID: PMC5838594.
51. Finnerty BM, Gray KD, Ullmann TM, Zarnegar R, Fahey TJ, 3rd, Beninato T. Frailty is More Predictive than Age for Complications After Thyroidectomy for Multinodular Goiter. World J Surg. 2020;44(6):1876-84. Epub 2020/02/14. doi: 10.1007/s00268-020-05422-4. PubMed PMID: 32052107.
52. Samlan RA, Black MA, Abidov M, Mohler J, Fain M. Frailty Syndrome, Cognition, and Dysphonia in the Elderly. J Voice. 2020;34(1):160 e15- e23. Epub 2018/07/30. doi: 10.1016/j.jvoice.2018.06.001. PubMed PMID: 30055984.
53. Stojadinovic A, Shaha AR, Orlikoff RF, Nissan A, Kornak M-F, Singh B, Boyle JO, Shah JP, Brennan MF, Kraus DH. Prospective functional voice assessment in patients undergoing thyroid surgery. Annals of surgery. 2002;236(6):823-32.
54. Vidal Fortuny J, Guigard S, Karenovics W, Triponez F. Surgery of the thyroid: recent developments and perspective. Swiss medical weekly. 2015;145:w14144.
55. Lee JC, Breen D, Scott A, Grodski S, Yeung M, Johnson W, Serpell J. Quantitative study of voice dysfunction after thyroidectomy. Surgery. 2016;160(6):1576-81.
56. Hong KH, Kim YK. Phonatory characteristics of patients undergoing thyroidectomy without laryngeal nerve injury. Otolaryngology-Head and Neck Surgery. 1997;117(4):399-404.
57. Lombardi CP, Raffaelli M, De Crea C, D'alatri L, Maccora D, Marchese MR, Paludetti G, Bellantone R. Long-term outcome of functional post-thyroidectomy voice and swallowing symptoms. Surgery. 2009;146(6):1174-81.
58. Lombardi CP, Raffaelli M, D'Alatri L, Marchese MR, Rigante M, Paludetti G, Bellantone R. Voice and swallowing changes after thyroidectomy in patients without inferior laryngeal nerve injuries. Surgery. 2006;140(6):1026-34.
59. Sinagra DL, Montesinos MR, Tacchi VA, Moreno JC, Falco JE, Mezzadri NA, Debonis DL, Curutchet HP. Voice changes after thyroidectomy without recurrent laryngeal nerve injury. Journal of the American College of Surgeons. 2004;199(4):556-60.
60. Soylu L, Ozbas S, Uslu HY, Kocak S. The evaluation of the causes of subjective voice disturbances after thyroid surgery. The American Journal of Surgery. 2007;194(3):317-22.
61. Rulli F, Ambrogi V, Dionigi G, Amirhassankhani S, Mineo T, Ottaviani F, Buemi A, Di Stefano P, Mourad M. Meta-analysis of recurrent laryngeal nerve injury in thyroid surgery with or without intraoperative nerve monitoring. Acta Otorhinolaryngologica Italica. 2014;34(4):223.
62. Barczyński M, Randolph GW, Cernea CR, Dralle H, Dionigi G, Alesina PF, Mihai R, Finck C, Lombardi D, Hartl DM. External branch of the superior laryngeal nerve monitoring during thyroid and parathyroid surgery: International Neural Monitoring Study Group standards guideline statement. The Laryngoscope. 2013;123(S4).
63. Debruyne F, Ostyn F, Delaere P, Wellens W. Acoustic analysis of the speaking voice after thyroidectomy. J Voice. 1997;11(4):479-82. Epub 1998/01/09. doi: 10.1016/s0892-1997(97)80046-x. PubMed PMID: 9422284.

64. McIvor NP, Flint DJ, Gillibrand J, Morton RP. Thyroid surgery and voice-related outcomes. Aust N Z J Surg. 2000;70(3):179-83. Epub 2000/04/15. doi: 10.1046/j.1440-1622.2000.01781.x. PubMed PMID: 10765899.
65. Sinagra DL, Montesinos MR, Tacchi VA, Moreno JC, Falco JE, Mezzadri NA, Debonis DL, Curutchet HP. Voice changes after thyroidectomy without recurrent laryngeal nerve injury. J Am Coll Surg. 2004;199(4):556-60. Epub 2004/09/30. doi: 10.1016/j.jamcollsurg.2004.06.020. PubMed PMID: 15454138.
66. Stojadinovic A, Shaha AR, Orlikoff RF, Nissan A, Kornak MF, Singh B, Boyle JO, Shah JP, Brennan MF, Kraus DH. Prospective functional voice assessment in patients undergoing thyroid surgery. Ann Surg. 2002;236(6):823-32. Epub 2002/11/28. doi: 10.1097/00000658-200212000-00015. PubMed PMID: 12454521; PMCID: PMC1422649.
67. Papadakis CE, Asimakopoulou P, Proimos E, Perogamvrakis G, Papoutsaki E, Chimona T. Subjective and Objective Voice Assessments After Recurrent Laryngeal Nerve-Preserved Total Thyroidectomy. Journal of Voice. 2017.
68. Grogan RH, Aschebrook-Kilfoy B, Angelos P. Interventions to improve thyroid cancer survivors' quality of life. Future Medicine; 2016.
69. Sahli Z, Canner JK, Najjar O, Schneider EB, Prescott JD, Russell JO, Tufano RP, Zeiger MA, Mathur A. Association Between Age and Patient-Reported Changes in Voice and Swallowing After Thyroidectomy. Laryngoscope. 2019;129(2):519-24. Epub 2018/09/09. doi: 10.1002/lary.27297. PubMed PMID: 30194684; PMCID: PMC6344315.
70. Lombardi CP, Raffaelli M, D'Alatri L, Marchese MR, Rigante M, Paludetti G, Bellantone R. Voice and swallowing changes after thyroidectomy in patients without inferior laryngeal nerve injuries. Surgery. 2006;140(6):1026-32; discussion 32-4. Epub 2006/12/26. doi: 10.1016/j.surg.2006.08.008. PubMed PMID: 17188153.
71. Lortie CL, Thibeault M, Guitton MJ, Tremblay P. Effects of age on the amplitude, frequency and perceived quality of voice. Age (Dordr). 2015;37(6):117. Epub 2015/11/19. doi: 10.1007/s11357-015-9854-1. PubMed PMID: 26578457; PMCID: PMC5005868.
72. Kendall K. Presbyphonia: a review. Curr Opin Otolaryngol Head Neck Surg. 2007;15(3):137-40. Epub 2007/05/08. doi: 10.1097/MOO.0b013e328166794f. PubMed PMID: 17483679.
73. Christmas C, Rogus-Pulia N. Swallowing Disorders in the Older Population. J Am Geriatr Soc. 2019;67(12):2643-9. Epub 2019/08/21. doi: 10.1111/jgs.16137. PubMed PMID: 31430395; PMCID: PMC7102894.
74. Kuhn MA, Bloom G, Myssiorek D. Patient perspectives on dysphonia after thyroidectomy for thyroid cancer. Journal of Voice. 2013;27(1):111-4.
75. Gohrbandt AE, Aschoff A, Gohrbandt B, Keilmann A, Lang H, Musholt TJ. Changes of Laryngeal Mobility and Symptoms Following Thyroid Surgery: 6-Month Follow-Up. World journal of surgery. 2016;40(3):636-43.
76. Krekeler BN, Wendt E, Macdonald C, Orne J, Francis DO, Sippel R, Connor NP. Patient-Reported Dysphagia After Thyroidectomy: A Qualitative Study. JAMA Otolaryngol Head Neck Surg. 2018;144(4):342-8. Epub 2018/03/10. doi: 10.1001/jamaoto.2017.3378. PubMed PMID: 29522149; PMCID: PMC5876907.
77. Ortman JM, Velkoff VA, Hogan H. An aging nation: the older population in the United States. Washington, DC: US Census Bureau. 2014:25-1140.

78. Sosa JA, Hanna JW, Robinson KA, Lanman RB. Increases in thyroid nodule fine-needle aspirations, operations, and diagnoses of thyroid cancer in the United States. Surgery. 2013;154(6):1420-7.
79. Sura L, Madhavan A, Carnaby G, Crary MA. Dysphagia in the elderly: management and nutritional considerations. Clinical interventions in aging. 2012;7:287.
80. Takeuchi K, Aida J, Ito K, Furuta M, Yamashita Y, Osaka K. Nutritional status and dysphagia risk among community-dwelling frail older adults. The journal of nutrition, health & aging. 2014;18(4):352-7.
81. Mcivor NP, Flint DJ, Gillibrand J, Morton RP. THYROID SURGERY AND VOICE-RELATED OUTCOMES. Australian and New Zealand Journal of Surgery. 2000;70(3):179-83.
82. Echternach M, Maurer C, Mencke T, Schilling M, Verse T, Richter B. Laryngeal complications after thyroidectomy: is it always the surgeon? Archives of surgery. 2009;144(2):149-53.
83. Kovatch KJ, Reyes-Gastelum D, Hughes DT, Hamilton AS, Ward KC, Haymart MR. Assessment of Voice Outcomes Following Surgery for Thyroid Cancer. JAMA Otolaryngol Head Neck Surg. 2019. Epub 2019/07/19. doi: 10.1001/jamaoto.2019.1737. PubMed PMID: 31318375; PMCID: PMC6646991.
84. Akyildiz S, Ogut F, Akyildiz M, Engin EZ. A multivariate analysis of objective voice changes after thyroidectomy without laryngeal nerve injury. Arch Otolaryngol Head Neck Surg. 2008;134(6):596-602. Epub 2008/06/19. doi: 10.1001/archotol.134.6.596. PubMed PMID: 18559725.
85. Hodge FS, Colton RH, Kelley RT. Vocal intensity characteristics in normal and elderly speakers. J Voice. 2001;15(4):503-11. Epub 2002/01/17. doi: 10.1016/S0892-1997(01)00050-9. PubMed PMID: 11792026.
86. Galluzzi F, Garavello W. Dysphagia following uncomplicated thyroidectomy: a systematic review. Eur Arch Otorhinolaryngol. 2019;276(10):2661-71. Epub 2019/08/16. doi: 10.1007/s00405-019-05599-y. PubMed PMID: 31414222.
87. Gohrbandt AE, Aschoff A, Gohrbandt B, Keilmann A, Lang H, Musholt TJ. Changes of Laryngeal Mobility and Symptoms Following Thyroid Surgery: 6-Month Follow-Up. World J Surg. 2016;40(3):636-43. Epub 2015/11/13. doi: 10.1007/s00268-015-3323-y. PubMed PMID: 26560148.
88. Hyun K, Byon W, Park HJ, Park Y, Park C, Yun JS. Comparison of swallowing disorder following gasless transaxillary endoscopic thyroidectomy versus conventional open thyroidectomy. Surg Endosc. 2014;28(6):1914-20. Epub 2014/01/28. doi: 10.1007/s00464-013-3413-6. PubMed PMID: 24464386.
89. Lombardi CP, Raffaelli M, De Crea C, D'Alatri L, Maccora D, Marchese MR, Paludetti G, Bellantone R. Long-term outcome of functional post-thyroidectomy voice and swallowing symptoms. Surgery. 2009;146(6):1174-81. Epub 2009/12/05. doi: 10.1016/j.surg.2009.09.010. PubMed PMID: 19958946.
90. Cusimano A, Macaione I, Fiorentino E. How uncomplicated total thyroidectomy could aggravate the laryngopharyngeal reflux disease? Eur Arch Otorhinolaryngol. 2016;273(1):197-202. Epub 2015/01/09. doi: 10.1007/s00405-014-3474-8. PubMed PMID: 25567342.
91. Augustin T, Burstein MD, Schneider EB, Morris-Stiff G, Wey J, Chalikonda S, Walsh RM. Frailty predicts risk of life-threatening complications and mortality after pancreatic

resections. Surgery. 2016;160(4):987-96. Epub 2016/08/23. doi: 10.1016/j.surg.2016.07.010. PubMed PMID: 27545992.
92. Farhat JS, Velanovich V, Falvo AJ, Horst HM, Swartz A, Patton JH, Jr., Rubinfeld IS. Are the frail destined to fail? Frailty index as predictor of surgical morbidity and mortality in the elderly. J Trauma Acute Care Surg. 2012;72(6):1526-30; discussion 30-1. Epub 2012/06/15. doi: 10.1097/TA.0b013e3182542fab. PubMed PMID: 22695416.
93. Gajdos C, Kile D, Hawn MT, Finlayson E, Henderson WG, Robinson TN. Advancing age and 30-day adverse outcomes after nonemergent general surgeries. J Am Geriatr Soc. 2013;61(9):1608-14. Epub 2013/08/10. doi: 10.1111/jgs.12401. PubMed PMID: 23927841; PMCID: PMC4119758.
94. Robinson TN, Wallace JI, Wu DS, Wiktor A, Pointer LF, Pfister SM, Sharp TJ, Buckley MJ, Moss M. Accumulated frailty characteristics predict postoperative discharge institutionalization in the geriatric patient. J Am Coll Surg. 2011;213(1):37-42; discussion -4. Epub 2011/03/26. doi: 10.1016/j.jamcollsurg.2011.01.056. PubMed PMID: 21435921; PMCID: PMC3132184.
95. Robinson TN, Wu DS, Stiegmann GV, Moss M. Frailty predicts increased hospital and six-month healthcare cost following colorectal surgery in older adults. Am J Surg. 2011;202(5):511-4. Epub 2011/09/06. doi: 10.1016/j.amjsurg.2011.06.017. PubMed PMID: 21890098; PMCID: PMC3346286.
96. Bureau USC. National Population Projection Tables 2017 [cited 2018].
97. Lim H, Devesa SS, Sosa JA, Check D, Kitahara CM. Trends in Thyroid Cancer Incidence and Mortality in the United States, 1974-2013. JAMA. 2017;317(13):1338-48. doi: 10.1001/jama.2017.2719. PubMed PMID: 28362912.
98. Ito Y, Miyauchi A, Kihara M, Higashiyama T, Kobayashi K, Miya A. Patient age is significantly related to the progression of papillary microcarcinoma of the thyroid under observation. Thyroid. 2014;24(1):27-34. doi: 10.1089/thy.2013.0367. PubMed PMID: 24001104; PMCID: PMC3887422.
99. Wang Z, Vyas CM, Van Benschoten O, Nehs MA, Moore FD, Jr., Marqusee E, Krane JF, Kim MI, Heller HT, Gawande AA, Frates MC, Doubilet PM, Doherty GM, Cho NL, Cibas ES, Benson CB, Barletta JA, Zavacki AM, Larsen PR, Alexander EK, Angell TE. Quantitative Analysis of the Benefits and Risk of Thyroid Nodule Evaluation in Patients >/=70 Years Old. Thyroid. 2018;28(4):465-71. doi: 10.1089/thy.2017.0655. PubMed PMID: 29608439.
100. Jegerlehner S, Bulliard JL, Aujesky D, Rodondi N, Germann S, Konzelmann I, Chiolero A, Group NW. Overdiagnosis and overtreatment of thyroid cancer: A population-based temporal trend study. PLoS One. 2017;12(6):e0179387. doi: 10.1371/journal.pone.0179387. PubMed PMID: 28614405; PMCID: PMC5470703.
101. Lerch H, Schober O, Kuwert T, Saur HB. Survival of differentiated thyroid carcinoma studied in 500 patients. J Clin Oncol. 1997;15(5):2067-75. doi: 10.1200/JCO.1997.15.5.2067. PubMed PMID: 9164219.
102. Orosco RK, Hussain T, Brumund KT, Oh DK, Chang DC, Bouvet M. Analysis of age and disease status as predictors of thyroid cancer-specific mortality using the Surveillance, Epidemiology, and End Results database. Thyroid. 2015;25(1):125-32. doi: 10.1089/thy.2014.0116. PubMed PMID: 25369076; PMCID: PMC4291211.
103. Dellal FD, Ozdemir D, Tam AA, Baser H, Tatli Dogan H, Parlak O, Ersoy R, Cakir B. Clinicopathological features of thyroid cancer in the elderly compared to younger

counterparts: single-center experience. J Endocrinol Invest. 2017;40(5):471-9. doi: 10.1007/s40618-016-0577-7. PubMed PMID: 27885512.
104. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, Pacini F, Randolph GW, Sawka AM, Schlumberger M, Schuff KG, Sherman SI, Sosa JA, Steward DL, Tuttle RM, Wartofsky L. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid. 2016;26(1):1-133. Epub 2015/10/16. doi: 10.1089/thy.2015.0020. PubMed PMID: 26462967; PMCID: PMC4739132.
105. Hauber AB, Gonzalez JM, Groothuis-Oudshoorn CG, Prior T, Marshall DA, Cunningham C, MJ IJ, Bridges JF. Statistical Methods for the Analysis of Discrete Choice Experiments: A Report of the ISPOR Conjoint Analysis Good Research Practices Task Force. Value Health. 2016;19(4):300-15. doi: 10.1016/j.jval.2016.04.004. PubMed PMID: 27325321.
106. Nathan H, Bridges JF, Schulick RD, Cameron AM, Hirose K, Edil BH, Wolfgang CL, Segev DL, Choti MA, Pawlik TM. Understanding surgical decision making in early hepatocellular carcinoma. J Clin Oncol. 2011;29(6):619-25. Epub 2011/01/06. doi: 10.1200/JCO.2010.30.8650. PubMed PMID: 21205759; PMCID: PMC4834708.
107. Nathan H, Segev DL, Bridges JF, Massie AB, Cameron AM, Hirose K, Schulick RD, Choti MA, Pawlik TM. Influence of nonclinical factors on choice of therapy for early hepatocellular carcinoma. Ann Surg Oncol. 2013;20(2):448-56. Epub 2012/09/04. doi: 10.1245/s10434-012-2619-5. PubMed PMID: 22941170.
108. Bouma BJ, van der Meulen JH, van den Brink RB, Arnold AE, Smidts A, Teunter LH, Lie KI, Tijssen JG. Variability in treatment advice for elderly patients with aortic stenosis: a nationwide survey in The Netherlands. Heart. 2001;85(2):196-201. doi: 10.1136/heart.85.2.196. PubMed PMID: 11156672; PMCID: PMC1729630.
109. Timmermans DR, Gooszen AW, Geelkerken RH, Tollenaar RA, Gooszen HG. Analysis of the variety in surgeons' decision strategies for the management of left colonic emergencies. Med Care. 1997;35(7):701-13. doi: 10.1097/00005650-199707000-00004. PubMed PMID: 9219497.
110. Morley JE, Vellas B, van Kan GA, Anker SD, Bauer JM, Bernabei R, Cesari M, Chumlea WC, Doehner W, Evans J, Fried LP, Guralnik JM, Katz PR, Malmstrom TK, McCarter RJ, Gutierrez Robledo LM, Rockwood K, von Haehling S, Vandewoude MF, Walston J. Frailty consensus: a call to action. J Am Med Dir Assoc. 2013;14(6):392-7. doi: 10.1016/j.jamda.2013.03.022. PubMed PMID: 23764209; PMCID: PMC4084863.
111. Segal JB, Chang HY, Du Y, Walston JD, Carlson MC, Varadhan R. Development of a Claims-based Frailty Indicator Anchored to a Well-established Frailty Phenotype. Med Care. 2017;55(7):716-22. doi: 10.1097/MLR.0000000000000729. PubMed PMID: 28437320; PMCID: PMC5471130.
112. de Bekker-Grob EW, Donkers B, Jonker MF, Stolk EA. Sample Size Requirements for Discrete-Choice Experiments in Healthcare: a Practical Guide. Patient. 2015;8(5):373-84. doi: 10.1007/s40271-015-0118-z. PubMed PMID: 25726010; PMCID: PMC4575371.
113. Marshall D, Bridges JF, Hauber B, Cameron R, Donnalley L, Fyie K, Johnson FR. Conjoint Analysis Applications in Health - How are Studies being Designed and Reported?: An Update on Current Practice in the Published Literature between 2005 and 2008. Patient.

2010;3(4):249-56. Epub 2012/01/26. doi: 10.2165/11539650-000000000-00000. PubMed PMID: 22273432.
114. Coast J, Al-Janabi H, Sutton EJ, Horrocks SA, Vosper AJ, Swancutt DR, Flynn TN. Using qualitative methods for attribute development for discrete choice experiments: issues and recommendations. Health Econ. 2012;21(6):730-41. Epub 2011/05/11. doi: 10.1002/hec.1739. PubMed PMID: 21557381.
115. Janssen EM, Dy SM, Meara AS, Kneuertz PJ, Presley CJ, Bridges JFP. Analysis of Patient Preferences in Lung Cancer - Estimating Acceptable Tradeoffs Between Treatment Benefit and Side Effects. Patient Prefer Adherence. 2020;14:927-37. Epub 2020/06/26. doi: 10.2147/PPA.S235430. PubMed PMID: 32581519; PMCID: PMC7276327.
116. Janssen EM, Segal JB, Bridges JF. A Framework for Instrument Development of a Choice Experiment: An Application to Type 2 Diabetes. Patient. 2016;9(5):465-79. Epub 2016/04/28. doi: 10.1007/s40271-016-0170-3. PubMed PMID: 27120338.
117. Bridges JFP, Tsai JH, Janssen E, Crossnohere NL, Fischer R, Peay H. How Do Members of the Duchenne and Becker Muscular Dystrophy Community Perceive a Discrete-Choice Experiment Incorporating Uncertain Treatment Benefit? An Application of Research as an Event. Patient. 2019;12(2):247-57. Epub 2018/09/28. doi: 10.1007/s40271-018-0330-8. PubMed PMID: 30259384.
118. Richardson DR, Crossnohere NL, Seo J, Estey E, O'Donoghue B, Smith BD, Bridges JFP. Age at Diagnosis and Patient Preferences for Treatment Outcomes in AML: A Discrete Choice Experiment to Explore Meaningful Benefits. Cancer Epidemiol Biomarkers Prev. 2020;29(5):942-8. Epub 2020/03/07. doi: 10.1158/1055-9965.EPI-19-1277. PubMed PMID: 32132149; PMCID: PMC7196442.
119. Seo J, Smith BD, Estey E, Voyard E, B OD, Bridges JFP. Developing an instrument to assess patient preferences for benefits and risks of treating acute myeloid leukemia to promote patient-focused drug development. Curr Med Res Opin. 2018;34(12):2031-9. Epub 2018/03/23. doi: 10.1080/03007995.2018.1456414. PubMed PMID: 29565196.
120. Nathan H, Herlong HF, Gurakar A, Li Z, Koteish AA, Bridges JF, Pawlik TM. Clinical decision-making by gastroenterologists and hepatologists for patients with early hepatocellular carcinoma. Ann Surg Oncol. 2014;21(6):1844-51. Epub 2014/02/14. doi: 10.1245/s10434-014-3536-6. PubMed PMID: 24522993.
121. Reed Johnson F, Lancsar E, Marshall D, Kilambi V, Muhlbacher A, Regier DA, Bresnahan BW, Kanninen B, Bridges JF. Constructing experimental designs for discrete-choice experiments: report of the ISPOR Conjoint Analysis Experimental Design Good Research Practices Task Force. Value Health. 2013;16(1):3-13. Epub 2013/01/23. doi: 10.1016/j.jval.2012.08.2223. PubMed PMID: 23337210.
122. Ho AS, Luu M, Zalt C, Morris LGT, Chen I, Melany M, Ali N, Patio C, Chen Y, Mallen St-Clair J, Braunstein GD, Sacks WL, Zumsteg ZS. Mortality Risk of Nonoperative Papillary Thyroid Carcinoma: A Corollary for Active Surveillance. Thyroid. 2019;29(10):1409-17. Epub 2019/08/14. doi: 10.1089/thy.2019.0060. PubMed PMID: 31407637.
123. Shi LY, Liu J, Yu LJ, Lei YM, Leng SX, Zhang HY. Clinic-pathologic Features and Prognostic Analysis of Thyroid Cancer in the Older Adult: A SEER Based Study. J Cancer. 2018;9(15):2744-50. Epub 2018/08/09. doi: 10.7150/jca.24625. PubMed PMID: 30087716; PMCID: PMC6072817.
124. Ito Y, Miyauchi A, Kudo T, Higashiyama T, Masuoka H, Kihara M, Miya A. Kinetic Analysis of Growth Activity in Enlarging Papillary Thyroid Microcarcinomas. Thyroid.

2019;29(12):1765-73. Epub 2019/10/28. doi: 10.1089/thy.2019.0396. PubMed PMID: 31650907; PMCID: PMC6918870.
125. Tuttle RM, Fagin JA, Minkowitz G, Wong RJ, Roman B, Patel S, Untch B, Ganly I, Shaha AR, Shah JP, Pace M, Li D, Bach A, Lin O, Whiting A, Ghossein R, Landa I, Sabra M, Boucai L, Fish S, Morris LGT. Natural History and Tumor Volume Kinetics of Papillary Thyroid Cancers During Active Surveillance. JAMA Otolaryngol Head Neck Surg. 2017;143(10):1015-20. Epub 2017/09/01. doi: 10.1001/jamaoto.2017.1442. PubMed PMID: 28859191; PMCID: PMC5710258.
126. Adam MA, Thomas S, Youngwirth L, Hyslop T, Reed SD, Scheri RP, Roman SA, Sosa JA. Is There a Minimum Number of Thyroidectomies a Surgeon Should Perform to Optimize Patient Outcomes? Ann Surg. 2017;265(2):402-7. Epub 2017/01/07. doi: 10.1097/SLA.0000000000001688. PubMed PMID: 28059969.
127. Bech M, Gyrd-Hansen D. Effects coding in discrete choice experiments. Health Econ. 2005;14(10):1079-83. Epub 2005/04/27. doi: 10.1002/hec.984. PubMed PMID: 15852455.
128. Mohanty S, Rosenthal RA, Russell MM, Neuman MD, Ko CY, Esnaola NF. Optimal Perioperative Management of the Geriatric Patient: A Best Practices Guideline from the American College of Surgeons NSQIP and the American Geriatrics Society. J Am Coll Surg. 2016;222(5):930-47. Epub 2016/04/07. doi: 10.1016/j.jamcollsurg.2015.12.026. PubMed PMID: 27049783.
129. Haymart MR, Banerjee M, Yang D, Stewart AK, Sisson JC, Koenig RJ, Doherty GM, Griggs JJ. Variation in the management of thyroid cancer. J Clin Endocrinol Metab. 2013;98(5):2001-8. Epub 2013/03/30. doi: 10.1210/jc.2012-3355. PubMed PMID: 23539722; PMCID: PMC3644603.
130. Nixon IJ, Ganly I, Patel SG, Palmer FL, Whitcher MM, Tuttle RM, Shaha A, Shah JP. Thyroid lobectomy for treatment of well differentiated intrathyroid malignancy. Surgery. 2012;151(4):571-9. Epub 2011/10/18. doi: 10.1016/j.surg.2011.08.016. PubMed PMID: 22001636.
131. Harries V, Wang LY, McGill M, Xu B, Tuttle RM, Wong RJ, Shaha AR, Shah JP, Ghossein R, Patel SG, Ganly I. Should multifocality be an indication for completion thyroidectomy in papillary thyroid carcinoma? Surgery. 2020;167(1):10-7. Epub 2019/09/14. doi: 10.1016/j.surg.2019.03.031. PubMed PMID: 31515125; PMCID: PMC6904525.
132. Dhir M, McCoy KL, Ohori NP, Adkisson CD, LeBeau SO, Carty SE, Yip L. Correct extent of thyroidectomy is poorly predicted preoperatively by the guidelines of the American Thyroid Association for low and intermediate risk thyroid cancers. Surgery. 2018;163(1):81-7. Epub 2017/11/13. doi: 10.1016/j.surg.2017.04.029. PubMed PMID: 29128185.
133. Bilimoria KY, Bentrem DJ, Ko CY, Stewart AK, Winchester DP, Talamonti MS, Sturgeon C. Extent of surgery affects survival for papillary thyroid cancer. Ann Surg. 2007;246(3):375-81; discussion 81-4. Epub 2007/08/25. doi: 10.1097/SLA.0b013e31814697d9. PubMed PMID: 17717441; PMCID: PMC1959355.
134. Miyauchi A, Kudo T, Ito Y, Oda H, Yamamoto M, Sasai H, Higashiyama T, Masuoka H, Fukushima M, Kihara M, Miya A. Natural history of papillary thyroid microcarcinoma: Kinetic analyses on tumor volume during active surveillance and before presentation. Surgery. 2019;165(1):25-30. Epub 2018/11/11. doi: 10.1016/j.surg.2018.07.045. PubMed PMID: 30413323.

135. Adam MA, Goffredo P, Youngwirth L, Scheri RP, Roman SA, Sosa JA. Same thyroid cancer, different national practice guidelines: When discordant American Thyroid Association and National Comprehensive Cancer Network surgery recommendations are associated with compromised patient outcome. Surgery. 2016;159(1):41-50. Epub 2015/10/06. doi: 10.1016/j.surg.2015.04.056. PubMed PMID: 26435426.
136. Francis DO, Randolph G, Davies L. Nationwide Variation in Rates of Thyroidectomy Among US Medicare Beneficiaries. JAMA Otolaryngol Head Neck Surg. 2017;143(11):1122-5. Epub 2017/10/20. doi: 10.1001/jamaoto.2017.1746. PubMed PMID: 29049468; PMCID: PMC5710444.
137. Haymart MR, Esfandiari NH, Stang MT, Sosa JA. Controversies in the Management of Low-Risk Differentiated Thyroid Cancer. Endocr Rev. 2017;38(4):351-78. Epub 2017/06/22. doi: 10.1210/er.2017-00067. PubMed PMID: 28633444; PMCID: PMC5546880.

APPENDIX A. Voice Handicap Index (VHI)

VOICE HANDICAP INDEX

Name: _____ Date: _____

These are statements that many people have used to describe their voices and the effects of their voices on their lives. Circle the response that indicates how frequently you have the same experience.

0-never 1-almost never 2-sometimes 3-almost always 4-always

Part I-F

My voice makes it difficult for people to hear me.	0	1	2	3	4
People have difficulty understanding me in a noisy room.	0	1	2	3	4
My family has difficulty hearing me when I call them throughout the house.	0	1	2	3	4
I use the phone less often than I would like to.	0	1	2	3	4
I tend to avoid groups of people because of my voice.	0	1	2	3	4
I speak with friends, neighbors, or relatives less often because of my voice.	0	1	2	3	4
People ask me to repeat myself when speaking face-to-face.	0	1	2	3	4
My voice difficulties restrict my personal and social life.	0	1	2	3	4
I feel left out of conversations because of my voice.	0	1	2	3	4
My voice problem causes me to lose income.	0	1	2	3	4

SUBTOTAL _____

Part II-P

I run out of air when I talk.	0	1	2	3	4
The sound of my voice varies throughout the day.	0	1	2	3	4
People ask, "What's wrong with your voice?"	0	1	2	3	4
My voice sounds creaky and dry.	0	1	2	3	4
I feel as though I have to strain to produce voice.	0	1	2	3	4
The clarity of my voice is unpredictable.	0	1	2	3	4
I try to change my voice to sound different.	0	1	2	3	4
I use a great deal of effort to speak.	0	1	2	3	4
My voice is worse in the evening.	0	1	2	3	4
My voice "gives out" on me in the middle of speaking.	0	1	2	3	4

SUBTOTAL _____

Part III-E

I am tense when talking to others because of my voice.	0	1	2	3	4
People seem irritated with my voice.	0	1	2	3	4
I find other people don't understand my voice problem.	0	1	2	3	4
My voice problem upsets me.	0	1	2	3	4
I am less outgoing because of my voice problem.	0	1	2	3	4
My voice makes me feels handicapped.	0	1	2	3	4
I feel annoyed when people ask me to repeat.	0	1	2	3	4
I feel embarrassed when people ask me to repeat.	0	1	2	3	4
My voice makes me feel incompetent.	0	1	2	3	4
I am ashamed of my voice problem.	0	1	2	3	4

SUBTOTAL _____

TOTAL _____

APPENDIX B. Dysphagia Handicap Survey (DHI)

		Never	Sometimes	Always
1	I feel a discomfort when I swallow			
2	The food sticks or stays blocked in my throat			
3	I have difficulty swallowing liquids			
4	I cough or clear my throat during or after a meal			
5	I suffocate when eating or drinking			
6	I feel food or liquid coming up after a meal			
7	I have difficulty chewing			
8	Food comes up to my nose when I drink or eat			
9	I dribble when I eat			
10	My throat hurts when I swallow			
11	I am unable to eat certain foods because of my swallowing difficulties			
12	I have to modify the consistency of the food in order to swallow			
13	It takes longer to eat a meal because of my swallowing difficulties			
14	I eat less because of my swallowing problems			
15	I am still hungry or thirsty after a meal			
16	I am tired because of my swallowing problems			
17	I have lost weight because of my swallowing difficulties			
18	I am afraid of eating			
19	I have had bronchitis or pulmonary infections more often since my swallowing problems			
20	I have more trouble breathing since my swallowing problems			
21	I avoid eating with others because of my swallowing difficulties			
22	My swallowing problem limits my personal or social life			
23	I am bothered by the way I eat during a meal			
24	Eating has become disagreeable			
25	My swallowing difficulty constrains me			
26	I find that other do not understand my swallowing problems			
27	Others seem to be irritated by my swallowing problems			
28	I am tense when I eat with others because of my swallowing			
29	I am ashamed of my swallowing problem			
30	I feel handicapped because of my swallowing difficulties			

Thyroid Cancer in Older Adults - AAES

Start of Block: Demographics

Q36 **Instructions:** We are interested in learning about the thought processes and experiences of surgeons involved in deciding upon and performing thyroid surgery in older adults with thyroid cancer. There are 3 sections in this survey. In this first set of 10 questions we would like to learn about you and your practice.

Q1 Q1. What gender do you identify as?

- Male (1)
- Female (2)
- Other (3)

Q2 Q2. Please indicate your age

_____

Q3 Q3. Are you of Hispanic, Latino, or Spanish origin or descent?

- Yes (1)
- No (2)

Q4 Q4. Which of the following categories best describes your race? ***Please choose all that apply***

- ☐ American Indian or Alaskan Native (1)
- ☐ Asian (2)
- ☐ Black or African American (3)
- ☐ Native Hawaiian or Other Pacific Islander (4)
- ☐ White (5)
- ☐ Other (6)

Display This Question:

If Q4. Which of the following categories best describes your race? Please choose all that apply = Other

Q5 Please specify

_____

Q6 Q5. Please indicate your specialty

- ○ General Surgery (no fellowship training after residency) (1)
- ○ General Surgery and Endocrine Surgery Fellowship (2)
- ○ General Surgery and Surgical Oncology Fellowship (3)
- ○ Otolaryngology (no fellowship training after residency) (4)
- ○ Otolaryngology and Head & Neck/Endocrine Fellowship training (5)
- ○ Other (6)

Display This Question:

If Q5. Please indicate your specialty = Other

Q7 Please specify

_____

Q8 Q6. Please indicate your number of years in practice following completion of training (residency or fellowship if applicable)

_____

Q9 Q7. Thinking about the past two years, please indicate the approximate percentage of patients that you have operated on that are over the age of 65.

- ○ < 10% (1)
- ○ ≥10% but (2)
- ○ ≥25% but (3)
- ○ ≥50% (4)

Q10 Q8. Thinking about the past two years, is your practice limited to Endocrine Surgery only?

- ○ Yes (1)
- ○ No (2)

Display This Question:

If Q8. Thinking about the past two years, is your practice limited to Endocrine Surgery only? = No

Q11 Please indicate what percentage of your practice is limited to Endocrine Surgery (thyroid, parathyroid, adrenal, neuroendocrine)

- ○ < 10% (1)
- ○ ≥10% but (2)
- ○ ≥25% but (3)
- ○ ≥50% (4)

Q12 Q9. Thinking about the past two years, please indicate the approximate number of thyroid surgeries that you perform on average per year.

_____

Q13 Q10. Please select the type of hospital setting at which you primarily practice.

- ○ Community (1)
- ○ Community with an academic affiliation (2)
- ○ Academic with teaching (3)
- ○ Outpatient surgery only (4)
- ○ Other (5)

Display This Question:

If Q10. Please select the type of hospital setting at which you primarily practice. = Other

Q14 Please specify

_____

End of Block: Demographics

Start of Block: Block 1

Q37 In this second set of 6 questions we would like to learn about how you assess a patient's ability to tolerate surgery. **Please note that many of these questions will have multiple answers.**

Q15 Q1. Which of the following methods do you typically use to assess the ability of a patient age **less than 65** years to undergo thyroidectomy. ***Please choose all that apply***

- ☐ Overall clinical intuition about the patient when you first meet them (Eyeball test) (1)
- ☐ Chronological age (2)
- ☐ Number or type of co-morbidites (3)
- ☐ Estimate of functional status (4)
- ☐ Estimate of life expectancy (13)
- ☐ Calculate a co-morbidity index (Charlson, Elixhauser) (5)
- ☐ Calculate a frailty index (6)
- ☐ Number of medications (7)
- ☐ Anesthesia consult (8)
- ☐ Assessment by other providers based on co-morbidities- cardiologist, internist, pulmonologist, etc. (9)
- ☐ Presentation at tumor board (10)
- ☐ Opinion on a social media platform (facebook, ACS community board, etc.) (11)
- ☐ None of the above (12)

Q16 Q2. Which of the following methods do you typically use to assess the ability of a patient age **greater than 65** years to undergo thyroidectomy. ***Please choose all that apply***

- ☐ Overall clinical intuition about the patient when you first meet them (Eyeball test) (1)
- ☐ Chronological age (2)
- ☐ Number or type of co-morbidites (3)
- ☐ Estimate of functional status (4)
- ☐ Estimate of life expectancy (5)
- ☐ Calculate a co-morbidity index (Charlson, Elixhauser) (6)
- ☐ Calculate a frailty index (7)
- ☐ Number of medications (8)
- ☐ Anesthesia consult (9)
- ☐ Assessment by other providers based on co-morbidities- cardiologist, internist, pulmonologist, etc. (10)
- ☐ Refer to or have assessed by a geriatrician (11)
- ☐ Presentation at tumor board (12)
- ☐ Opinion on a social medial platform (facebook, ACS community board, etc.) (13)
- ☐ None of the above (14)

Carry Forward Selected Choices from "Q2. Which of the following methods do you typically use to assess the ability of a patient age greater than 65 years to undergo thyroidectomy. Please choose all that apply"

Q41 Q3. Of the following methods that you selected, how important are those items when you assess a patient's **(age 65-79)** ability to benefit from surgery?

	Extremely important (1)	Very important (2)	Moderately important (3)	Slightly important (4)
Overall clinical intuition about the patient when you first meet them (Eyeball test) (x1)	○	○	○	○
Chronological age (x2)	○	○	○	○
Number or type of co-morbidites (x3)	○	○	○	○
Estimate of functional status (x4)	○	○	○	○
Estimate of life expectancy (x5)	○	○	○	○
Calculate a co-morbidity index (Charlson, Elixhauser) (x6)	○	○	○	○
Calculate a frailty index (x7)	○	○	○	○
Number of medications (x8)	○	○	○	○
Anesthesia consult (x9)	○	○	○	○
Assessment by other providers based on co-morbidities- cardiologist, internist, pulmonologist, etc. (x10)	○	○	○	○
Refer to or have assessed by a geriatrician (x11)	○	○	○	○

Presentation at tumor board (x12)	○	○	○	○
Opinion on a social medial platform (facebook, ACS community board, etc.) (x13)	○	○	○	○
None of the above (x14)	○	○	○	○

Carry Forward Selected Choices from "Q2. Which of the following methods do you typically use to assess the ability of a patient age greater than 65 years to undergo thyroidectomy. Please choose all that apply"

Q42 Q4. Of the following methods that you selected, how important are those items when you assess a **≥ 80 year old** patient's ability to benefit from surgery?

	Extremely Important (1)	Very Important (2)	Moderately important (3)	Slightly important (4)
Overall clinical intuition about the patient when you first meet them (Eyeball test) (x1)	○	○	○	○
Chronological age (x2)	○	○	○	○
Number or type of co-morbidites (x3)	○	○	○	○
Estimate of functional status (x4)	○	○	○	○
Estimate of life expectancy (x5)	○	○	○	○
Calculate a co-morbidity index (Charlson, Elixhauser) (x6)	○	○	○	○
Calculate a frailty index (x7)	○	○	○	○
Number of medications (x8)	○	○	○	○
Anesthesia consult (x9)	○	○	○	○
Assessment by other providers based on co-morbidities- cardiologist, internist, pulmonologist, etc. (x10)	○	○	○	○
Refer to or have assessed by a geriatrician (x11)	○	○	○	○

Presentation at tumor board (x12)	○	○	○	○
Opinion on a social medial platform (facebook, ACS community board, etc.) (x13)	○	○	○	○
None of the above (x14)	○	○	○	○

Display This Question:

If Q1. Which of the following methods do you typically use to assess the ability of a patient age le... = Estimate of life expectancy

Or Q2. Which of the following methods do you typically use to assess the ability of a patient age gr... = Estimate of life expectancy

Q45 Q5. Please choose how many years ***at minimum*** that you consider to be a limited life expectancy AND therefore would not recommend any surgical intervention for an adult with thyroid cancer?

- ○ Life expectancy less than 1 year (1)
- ○ Life expectancy less than 3 years (2)
- ○ Life expectancy less than 5 years (3)
- ○ Life expectancy less than 10 years (4)
- ○ other (5)

Display This Question:

If Q5. Please choose how many years at minimum that you consider to be a limited life expectancy AND... = other

Q46 Please specify the number of years, at minimum, that you consider to be a limited life expectancy limiting your recommendation to no surgery.

_____

Q20 Q6. How often do you weigh the following considerations prior to providing a surgical opinion in a patient age > 65 with thyroid pathology

	Always (1)	Most of the time (2)	About half the time (3)	Sometimes (4)	Never (5)
Most thyroid cancer is slow growing and unlikely to cause mortality if untreated (1)	○	○	○	○	○
Thyroid cancer in older adults tends to be more aggressive (2)	○	○	○	○	○
Estimate of life-expectancy (3)	○	○	○	○	○
Co-morbidities will likely cause mortality prior to thyroid cancer (4)	○	○	○	○	○
Location of thyroid cancer (5)	○	○	○	○	○
Risk of anesthesia (6)	○	○	○	○	○
Discussion of patient goals regarding quality of life versus life-expectancy (7)	○	○	○	○	○
Presence of compressive symptoms (dysphagia or voice changes) (8)	○	○	○	○	○

Whether or not the patient is on synthroid (9)	○	○	○	○	○

End of Block: Block 1

Start of Block: Block 3

Q38 **Instructions:** The following questions present 3 case scenarios in several different patients. Please consider how you manage your own patients. What would you recommend for each?

Q48 A male presents with 2.5 cm palpable, mobile, right-sided PTC with no compressive symptoms. No suspicious lymph nodes are seen on ultrasound. He is euthyroid and has no family history of thyroid cancer or prior exposure to XRT. What would you recommend for each of the following patients?

	Management Options		
	Right thyroid lobectomy (1)	Total thyroidectomy (2)	Active Surveillance (3)

40 year old with diabetes, COPD, and hypertension. He lives alone and takes care of himself. (1)	○	○	○
58 year old healthy male (2)	○	○	○
74 year old with diabetes only. He lives alone and takes care of himself. (3)	○	○	○
92 year old with diabetes only. He lives alone and takes care of himself. (4)	○	○	○
60 year old with diabetes, hypertension s/p cardiac stent two years ago. He has lost 10 pounds in the past six months, reports poor energy, and therefore does not get out much. (7)	○	○	○
75 year old with COPD and diabetes. He reports poor energy and uses a walker for assistance. (5)	○	○	○
88 year old with hypertension and diabetes. He has lost 10 pounds in the past six months, reports poor energy, and therefore does not get out much. He walks with assistance. (6)	○	○	○

74 year old with hypertension, COPD, diabetes, congestive heart failure, and peripheral vascular disease s/p iliac artery stent. He lives alone and takes care of himself (8)	○	○	○

Q29 **A female has a 2.5cm palpable, mobile, right-sided PTC with no compressive symptoms. She has a 2cm right lateral (level III) neck node that also demonstrates PTC on biopsy. She is euthyroid and has no family history of thyroid cancer or prior exposure to XRT.**

	Management				
	Right thyroid lobectomy +/- central neck dissection (1)	Right thyroid lobectomy with central and right lateral neck dissection (2)	Total thyroidectomy +/- central neck dissection (3)	Total thyroidectomy with central and right lateral neck dissection (4)	Active-surveillance (5)

40 year old with diabetes, COPD, and hypertension. She lives alone and takes care of herself. (1)	○	○	○	○	○
59 year old healthy female (11)	○	○	○	○	○
75 year old with diabetes only. She lives alone and takes care of herself. (2)	○	○	○	○	○
89 year old with diabetes only. She lives alone and takes care of herself. (3)	○	○	○	○	○
62 year old with diabetes, hypertension s/p cardiac stent two years ago. She has lost 10 pounds in the past six months, reports poor energy, and therefore does not get out much. (9)	○	○	○	○	○

76 year old with diabetes, hypertension s/p cardiac stent two years ago. She has lost 10 pounds in the past six months, reports poor energy, and therefore does not get out much. (4)	○	○	○	○	○
88 year old with hypertension and diabetes. She has lost 10 pounds in the past six months, reports poor energy, and therefore does not get out much. She walks with assistance. (5)	○	○	○	○	○
74 year old with hypertension, COPD diabetes, congestive heart failure, and peripheral vascular disease s/p iliac artery stent. She lives alone and takes care of herself (6)	○	○	○	○	○

Q47 **A female has a 4.1 cm palpable, mobile, right-sided PTC with no compressive symptoms. No suspicious lymph nodes are seen on ultrasound. She is euthyroid and has no family history of thyroid cancer or prior exposure to XRT.**

	Management				
	Right thyroid lobectomy (1)	Right thyroid lobectomy + prophylactic central neck dissection (2)	Total thyroidectomy (3)	Total thyroidectomy + prophylactic central neck dissection (4)	Active Surveillance (5)

40 year old with diabetes, COPD, and hypertension. She lives alone and takes care of herself. (1)	○	○	○	○	○
75 year old with diabetes only. She lives alone and takes care of herself. (2)	○	○	○	○	○
89 year old with diabetes only. She lives alone and takes care of herself. (3)	○	○	○	○	○
62 year old with diabetes, hypertension s/p cardiac stent two years ago. She has lost 10 pounds in the past six months, reports poor energy, and therefore does not get out much. (4)	○	○	○	○	○

78 year old with diabetes, hypertension s/p cardiac stent two years ago. She has lost 10 pounds in the past six months, reports poor energy, and therefore does not get out much. (5)	○	○	○	○	○
88 year old with hypertension. She has lost 10 pounds in the past six months, reports poor energy, and therefore does not get out much. She walks with assistance. (6)	○	○	○	○	○
74 year old with hypertension, COPD, diabetes, congestive heart failure, and peripheral vascular disease. She lives alone and takes care of herself. (9)	○	○	○	○	○

End of Block: Block 3

Start of Block: Block 2

Q25 Prior to taking this survey, were you aware that the American College of Surgeons has a coalition on geriatric surgery?

- ○ yes (1)
- ○ No (2)

Display This Question:

If Prior to taking this survey, were you aware that the American College of Surgeons has a coalition... = yes

Q26 Prior to taking this survey, were you aware that this organization published best practice guidelines regarding optimal pre-operative assessment of the geriatric surgical patient?

- ○ Yes (1)
- ○ No (2)

Display This Question:

If Prior to taking this survey, were you aware that this organization published best practice guidel... = Yes

Q27 Do you routinely use this guideline in assessment of a geriatric surgical patient?

- ○ Yes (1)
- ○ No (2)

Q43 This now concludes the survey. Thank you for your participation. If you wish to be included in a raffle for an Amazon Gift Card, please enter your email address below. It will be separated from your survey responses to maintain anonymity.

_____

End of Block: Block 2

CURRICULUM VITAE
The Johns Hopkins University School of Medicine

Aarti Mathur, M.D, FACS April 23, 2021

DEMOGRAPHIC AND PERSONAL INFORMATION

Current Appointments

University

2020-Present	Associate Professor, Department of Surgery, Johns Hopkins University School of Medicine
2017-Present	Director, Endocrine Surgery Fellowship Program
2014-2020	Assistant Professor, Department of Surgery, Johns Hopkins University School of Medicine

Hospital

2014-Present	Attending Physician, Johns Hopkins Hospital
2016-Present	Attending Physician, Chief of Endocrine Surgery Sibley Memorial Hospital, Washington DC

Other
None

Personal Data

The Johns Hopkins Hospital
Division of Surgical Oncology, Department of Surgery
Blalock 606
600 N. Wolfe Street, Blalock 606
Baltimore, MD 21287
Phone: (410) 614-1197
Fax: (410) 502-1891
amathu10@jhmi.edu

Education and Training

Undergraduate

2000	B.A./University of Texas, Austin, TX

Doctoral/graduate

2004	M.D., University of Texas Medical Branch, Galveston, TX

Postdoctoral

2004-2005	Intern, General Surgery, Georgetown University, Washington, DC

2005-2007 Residency, General Surgery, Georgetown University, Washington, DC
2007-2011 Research Fellowship, Surgical Oncology, Dr. Steven A. Rosenberg, National Cancer Institute,
Bethesda, MD
2011-2013 Residency, General Surgery, Georgetown University, Washington, DC
2013-2014 Fellowship, Endocrine Surgery, Dr. Martha A. Zeiger, Johns Hopkins University, Baltimore, MD
2017–Present Ph.D., Graduate Training in Clinical Investigation Program, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD (Defense 2021)

Professional Experience
2014-Present Assistant Professor, General Surgery, Johns Hopkins University School of Medicine,
Baltimore, MD
2017-Present Director, Endocrine Surgery Fellowship Program, General Surgery, The Johns Hopkins University School of Medicine, Baltimore, MD

PUBLICATIONS:
Original Research [OR]

1. Johnson LA, Morgan RA, Dudley ME, Cassard L, Yang JC, Hughes MS, Kammula US, Royal RE, Sherry RM, Wunderlich JR, Lee CC, Restifo NP, Schwarz SL, Cogdill AP, Bishop RJ, Kim H, Brewer CC, Rudy SF, VanWaes C, Davis JL, **Mathur A**, Ripley RT, Nathan DA, Laurencot CM, Rosenberg SA. Gene Therapy with human and mouse T-cell receptors mediates cancer regression and targets normal tissues expressing cognate antigen. Blood. 2009; 114(3): 535-46. *I performed many of the critical experiments for this paper.*

2. Ripley RT, Davis JL, Klapper JA, **Mathur A**, Kammula U, Royal RE, Yang JC, Sherry RM, Hughes MS, Libutti SK, White DE, Steinberg SM, Dudley ME, Rosenberg SA, Avital I. Liver Resection for Metastatic Melanoma with Postoperative Tumor-Infiltrating Lymphocyte Therapy. Ann Surg Oncol. 2010; 17: 163-170. *I helped with data abstraction, analysis, and manuscript editing.*

3. Klapper JA, Davis JL, Ripley RT, Smith FO, Nguyen DM, Kwong KF, Mercedes L, Kemp CD, **Mathur A**, White DE, Dudley ME, Wunderlich JR, Rosenberg SA, Schrump DS. Thoracic metastasectomy for adoptive immunotherapy of melanoma: A single-institution experience. J Thorac Cardiovasc Surg. 2010; 1-7. *I helped collect and analyze the retrospective data*

4. Royal RE, Levy C, Turner K, **Mathur A,** Hughes M, Kammula US, Sherry RM, Topalian SL, Yang JC, Lowy I, Rosenberg SA. Phase 2 trial of single agent Ipilimumab (anti-CTLA-4) for locally advanced or metastatic pancreatic adenocarcinoma. J Immunotherapy. 2010; 33(8): 828-33. *I performed many of the critical experiments for this paper.*

5. **Mathur A**, Kemp CK, Dutta U, Baid S, Ayala A, Chang RE, Steinberg SM, Papademetrious V, Lange E, Libutti SK, Pingpank JF, Alexander HR, Phan GQ, Hughes M, Linehan WM, Pinto PA,

Stratakis CA, Kebebew E. Consequences of adrenal venous sampling in primary hyperaldosteronism and predictors of unilateral disease. J Am Coll Surg. 2010; 211 (3): 384-90.

6. **Mathur A**, Weng J, Moses W, Steinberg SM, Rahbari R, Kitano M, Khanafshar E, Ljung B, Duh Q, Clark OH, Kebebew E. A prospective trial evaluating the accuracy of using combined clinical factors and candidate diagnostic markers to refine the accuracy of thyroid fine needle aspiration biopsy. Surgery. 2010; 148(6): 1170-6.

7. Rahbari R, **Mathur A**, Kitano M, Guerrero M, Shen WT, Duh Q, Clark OH, Kebebew E. Prospective randomized trial of ligasure versus harmonic hemostasis technique in thyroidectomy. Annals of Surgical Oncology. 2011; 18(4): 1023-7. *I helped design the study, collect data, and helped with manuscript preparation.*

8. **Mathur A**, Moses W, Rahbari R, Khanafshar E, Duh QY, Clark O, Kebebew E. Higher Rate of BRAF mutation in papillary thyroid cancer over time: A single-institution study. Cancer. 2011; 117(19):4390-5.

9. Kemp CD, Ripley RT, **Mathur A**, Steinberg SM, Nguyen DM, Fojo T, Schrump DS. Pulmonary resection for metastatic adrenocortical carcinoma: the National Cancer Institute experience. Ann Thorac Surg. 2011; 92(4): 1195-1200. *I helped conceptualize the study as well as collect and analyze retrospective data*.

10. Kemp CD, Rao M, Inchauste S, Mani H, Fetsch P, Filie AC, Zhang M, Hong JA, Walker R, Zhu YJ, Ripley RT, **Mathur A**, Liu F, Yang M, Meltzer PS, Marquez VE, De Rienzo A, Bueno R, Schrump DS. Polycomb Repressor Complex-2 is a Novel Target for Mesothelioma Therapy. Clin Cancer Res. 2011; 18(1): 77-90. *I helped perform the experiments and edit the manuscript*

11. Webb R, **Mathur A**, Chang R, Baid S, Nilubol N, Libutti SK, Stratakis CA, Kebebew E. What is the best criterion for the interpretation of adrenal vein sample results in patients with primary hyperaldosteronism? Annals of Surgical Oncology. 2012; 19(6): 1881-6. *I helped conceptualize the study and assisted with collection and analysis of the data*

12. Zhang M, **Mathur A**, Zhang Y, Xi S, Atay S, Hong JA, Datrice N, Upham T, Kemp CD, Ripley RT, Wiegand G, Avital I, Fetsch P, Mani H, Zlott D, Robey R, Bates SE, LI x, Rao M, Schrump DS. Mithramycin represses basal and cigarette smoke-induced expression of ABCG2 and inhibits stem cell signaling in lung and esophageal cancer cells. Cancer Res. 2012; 72(16); 4178-92. *I helped design the study, performed most of the critical experiments for this paper, and assisted with manuscript preparation.*

13. Weisbrod AB, Webb RC, **Mathur A**, Barak S, Abraham SB, Nilubol N, Quezado M, Stratakis CA, Kebebew E. Adrenal histologic findings show no difference in clinical presentation and outcome in primary hyperaldosteronism. Ann Surg Oncol. 2013; 20(3): 753-8. *Helped with data collection and analysis*

14. **Mathur A**, Najafian A, Schneider EB, Zeiger MA, Olson MT. Malignancy risk and reproducibility associated with atypia of undetermined significance on thyroid cytology. Surgery. 2014; 156(6): 1471-6.

15. Noureldine SI, Najafian A, Aragon Han P, Olson MT, Genther DJ, Schneider EB, Prescott JD, Agrawal N, **Mathur A**, Zeiger MA, Tufano RP. Evaluation of the effect of diagnostic molecular testing on the surgical decision-making process for patients with thyroid nodules. JAMA Otolaryngol Head Neck Surg. 2016; Jul 142(7): 676-82. *I helped design the study, contributed patients towards this study and helped edit the manuscript*

16. Rowe SP, **Mathur A**, Bishop JA, Epstein JI, Prescott JD, Salvatori R, Siegelman SS, Fishman EK. CT Appearance of surgically resected adrenal hemorrhages. J of Computer Assisted Tomography. 2016; 40(6): 892-895. *I contributed patients and helped with data extraction and manuscript preparation*

17. Azoury SC, Nagarajan N, Young A, **Mathur A**, Prescott JD, Fishman EK, Zeiger MA. Computed Tomography in the management of adrenal tumors: Does size still matter? J Comput Assist Tomography. 2017; 41(4):628-632. *I contributed patients and helped with data extraction and manuscript preparation*

18. **Mathur A**, Nagarajan N, Kahan S, Schneider EB, Zeiger MA. Association of parathyroid hormone level with post-thyroidectomy hypocalcemia: A systematic-review. JAMA Surgery. 2018; 153(1):69-76.

19. Karipineni F, Sahli Z, Somervell H, **Mathur A**, Prescott JD, Tufano RP, Zeiger MA. Are preoperative sestamibi scans useful for identifying ectopic parathyroid glands in patients with expected multigland parathyroid disease? Surgery. 2018; 163(1):35-41. *I contributed patients and helped with data extraction and manuscript editing*

20. Sahli ZT, Najafian A, Kahan S, Schneider EB, Zeiger MA, **Mathur A**. One-hour postoperative parathyroid hormone levels do not reliably predict hypocalcemia after thyroidectomy. World J Surg. 2018; 42(7): 2128-2133.

21. Sahli ZT, Zhou S, Najjar O, Onasanya O, Segev D, Massie A, Zeiger MA, **Mathur A**. Octogenarians have worse clinical outcomes after thyroidectomy. Am J Surg. 2018; 216(6):1171-1176.

22. Sahli ZT, Ansari G, Gurakar M, Canner JK, Segev D, Zeiger MA, **Mathur A**. Thyroidectomy in older adults: an ACS-NSQIP study of outcomes. J Surgical Research. 2018; 229:20-27.

23. Sahli ZT, Canner JK, Najjar O, Schneider EB, Prescott JD, Russell JO, Tufano RP, Zeiger MA, **Mathur A**. Association between age and patient-reported changes in voice and swallowing after thyroidectomy. Laryngoscope. 2019; 129(2):519-524.

24. Trinh G, Rettig E, Noureldine SI, Russell JO, Agrawal N, **Mathur A**, Prescott JD, Zeiger MA, Tufano RP. Surgical management of normocalcemic primary hyperparathyroidism and the impact of intraoperative parathyroid hormone testing on outcome. Otolaryngol Head Neck Surg. 2018; 159(4): 630-637.
I contributed patients towards this study and helped to edit the manuscript.

25. Sahli ZT, Sharma AK, Canner JK, Karipineni F, Ali O, Kawamoto S, Hang J, **Mathur A**, Ali SZ, Zeiger MA, Sheth S. TIRADS inter-observer variability among indeterminate thyroid nodules – a single institution study. J Ultrasound in Medicine. 2019;38(7): 1807-1813. *I contributed patients and helped with study design, data extraction and manuscript preparation*

26. Sahli ZT, Karipineni F, Hang, Canner JK, **Mathur A**, Prescott JD, Sheth S, Ali SZ, Zeiger MA. The Association between Ultrasonography TIRADS Classification System and Surgical Pathology Among Indeterminate Thyroid Nodules. Surgery; 2019; 165(1):69-74. *I contributed patients and helped with study design, data extraction and manuscript preparation*

27. Karipineni F, Sahli ZT, Canner J, Somervell H, **Mathur A**, Prescott J, Tufano RP, Zeiger MA. Is cervical ultrasound to examine lymph nodes in patients with indeterminate or malignant subcentimeter thyroid nodules useful? J of Ultrasound in Medicine. 2019; 38(7): 1807-1813. *I contributed patients and helped with study design, data extraction and manuscript preparation*

28. DiBrito SR, Lopez CM, Jones C, **Mathur A**. Reducing Implicit Bias: Association of Women Surgeons #HeForShe Taskforce best practice recommendations. J Am Coll Surg 2019 Mar;228(3):303-309.

29. Sutton W, Canner JK, Rooper LM, Prescott JD, Zeiger MA, **Mathur A**. Is patient age associated with risk of malignancy in a ≥4cm cytologically benign thyroid nodule? The Am J of Surg. 2020; June (20)30347-0.

30. Sutton W, Canner JK, Segev DL, Zeiger MA, **Mathur A**. Treatment variation in older adults with differentiated thyroid cancer. J Surg Research. 2020; 254:154-164.

31. Chen LW, Razavi CR, Hong H, Fondong A, Ranganath R, Khatri S, Mydlarz WK, **Mathur A**, Ishii M, Nellis J, Shaear M, Tufano RP, Russell JO. Cosmetic outcomes following transoral versus transcervical thyroidectomy. Head Neck. 2020; 42(11):3336-3344. *I helped with data extraction and manuscript preparation.*

32. Sahli ZT, Canner JK, Zeiger MA, **Mathur A**. Association between age and disease specific mortality in Medullary thyroid cancer. Am J Surg. 2020;S0002-9610(20)30594-8.

33. Sahli ZT, Zeiger MA, **Mathur A**. Rising Cost of Thyroid Surgery in Adult Patients. J Surg Research 2020; 260: 28-37.

34. **Mathur A**, Sutton W, Ahn JB, Prescott JD, Zeiger MA, Segev DL, McAdams-DeMarco M. Association between treatment of secondary hyperparathyroidism and post-transplant outcomes. Transplantation. 2021. *Online ahead of print.*

35. Sutton W, Chen X, Patel P, Karzai S, Prescott JD, Segev DL, McAdams-DeMarco M, **Mathur A**. Prevalence and risk factors for tertiary hyperparathyroidism in kidney transplant recipients. Surgery. *In press*.

36. Karzai S, Zhang Z, Sutton W, Prescott JD, Segev DL, McAdams-DeMarco M, Biswal S, Ramanathan M, **Mathur A**. Ambient particulate matter air pollution is associated with increased risk of papillary thyroid cancer. Surgery. *In press*

Review Articles [RA]

1. **Mathur A**, Gorden P, Libutti SK. Insulinoma. Surg Clinics North Am. 2009; 89(5): 1105-1121.
2. **Mathur A**, Olson M, Zeiger M. Follicular Lesions of the Thyroid Gland. Surg Clin N Am. 2014; 94(3): 499-513.
3. **Mathur A,** Zeiger MA. Genomic medicine for cancer prognosis. J Surg Oncol. 2015; 111(1): 31-7.
4. **Mathur A,** Schneider EB, Zeiger MA. Is there an increased risk of second primary malignancy after diagnosis of thyroid cancer? Cancer. 2015; 121(2): 166-168.
5. Shank J, Prescott JD, **Mathur A**. Adrenal causes of Endocrine Hypertension: In: Endocrinology and Metabolism Clinics. 2019; 48(4):875-885.

Case Reports [CR]

1. Suffredini G, Diaz-Rodriguez N, Chakravarthy K, **Mathur A**, Hayanga HK, Frank SM, Ringel RE, Freiberg S, Barodka VM, Steppan J. Anesthetic management of pheochromocytoma resection in adults with single ventricle physiology. Cureus. 2017; 9(12):e1928. *This report was based off my patients and I helped with manuscript preparation and editing.*

2. Sharma AK, Sahli ZT, **Mathur A**. Bilateral chylothorax following re-operative central neck dissection for metastatic papillary thyroid cancer. BMJ Case Rep. 2018; 2018..

Book Chapters, Monographs [BC]

1. Weber D, **Mathur A**. Laparoscopic Splenectomy. In Stephen RT Evans (ed). Surgical Pitfalls. Saunders Elsevier, Philadelphia, 2008; 571-582.

2. **Mathur A**, Evans Stephen RT. Chest Tube Insertion. In Stephen RT Evans (ed). Surgical Pitfalls. Saunders Elsevier, Philadelphia, 2008; 135-142.

3. **Mathur A**, Kebebew E. Familial Non-medullary Thyroid Cancer. In Gregory Randolph (ed). Surgery of the Thyroid and Parathyroid Glands. Saunders Elsevier, Philadelphia, 2012; 265-269.

4. **Mathur A,** Dackiw AP. Nerve Monitoring during Thyroidectomy. In Orlo H. Clark, Quan-Yang Duh, and Electron Kebebew (ed). Textbook of Endocrine Surgery. Saunders Elsevier, Philadelphia, 2016;

5. Najafian A, **Mathur A,** Zeiger M. Molecular Profiles and the "Indeterminate" Thyroid Nodule. In: John B. Hanks and William B. Inabnet III (ed). Controversies in Thyroid Surgery, 2015. *I contributed to manuscript preparation and editing..*

6. Azoury SC, **Mathur A**. Primary Hyperaldosteronism. In: Electron Kebebew (ed). Management of Adrenal Masses in Children and Adults. Cham: Springer International Publishing, Illinois, 2017; 139-157.

7. Alobuia W, **Mathur A**, Kebebew E. Familial Non-medullary Thyroid Cancer. In: Gregory Randolph, Editor, Surgery of the Thyroid and Parathyroid Glands. Elsevier, New York, 2019; *I contributed to manuscript preparation and final editing..*

Books, Textbooks [BK]

None

Other Publications

None

FUNDING

EXTRAMURAL Funding

Research Extramural Funding - Current

4/1/2017 – 4/1/2022 Association between Frailty and Post-thyroidectomy Alterations in Voice, Swallowing, and Quality of Life.
1K23AG053429-01A1
NIA/NIH K23 Mentored Career Development Award
$847,445
Role: PI, 75%

Research Extramural Funding – Pending

7/1/2021 – 06/30/2026 D.E.C.I.D.E (DEcision-making mitigating Cognitive decline and Incident DEmentia) in Older Patients with Secondary Hyperparathyroidism
R01AG073228
NIA/NIH R01
$2,316,979
Role: PI

9/1/2021-8/31/2026 Optimizing Cardiovascular Health in End-Stage Renal Disease Patients with Secondary Hyperparathyroidism
R01HL000000
NHLBI/NIA R01

$3,828,894
Role: PI

Research Extramural Funding – Previous

8/1/2015-1/31/2018 Frailty and alterations in voice and swallowing after thyroidectomy
In older adults and the ability of frailty to predict these
Alterations
Older American Independence Center Pilot/Exploratory Studies
Core Award
Claude. D. Pepper Center (NIA)
$26,500
Role: PI

INTRAMURAL Funding

Research Intramural Funding – Current

1/1/2021-12/31/2021 Frailty and shared decision-making in older adults with thyroid cancer
Atterbury Discovery Grant
Johns Hopkins Thyroid Tumor Center
$30,000
Role: PI

Research Intramural Funding – Pending
None

Research Intramural Funding - Previous

1/1/2016-1/1/2017 Outcomes after thyroidectomy in older adults
Rothman Pilot Career Development Award
Johns Hopkins University School of Medicine Dept of Surgery,
$25,000
Role: PI, 10%

1/1/2016-1/1/2018 Association between frailty and outcomes after thyroidectomy in
Older adults
The Johns Hopkins Clinician-Scientist Award
$80,000
Role: PI, 75%

4/1/2016-12/31/2016 Outcomes in thyroidectomy in older adults vs. younger adults
Premier Healthcare Database
$10,000
Role: PI, 5%

CLINICAL ACTIVITIES
Clinical Focus

As a fellowship trained endocrine surgeon, my primary focus is on surgical management of thyroid, parathyroid, and adrenal disease. In addition to my clinical activities at JHH Baltimore, I have developed a tertiary care endocrine surgery presence in the National Capitol Region, drawing patients from Maryland, Washington DC, Delaware, and Virginia. I continue to be an active member of the Thyroid Tumor Center and the Adrenal Tumor Center at Johns Hopkins. Starting in March 2021, I will be Co-Director of the Johns Hopkins Thyroid Tumor Board.

Certification
None

Medical, other state/government licensure
8/2014-present State of Maryland Medical License (# D0078322); renewed 2016; 2018; 2020

6/2007-present District of Columbia Medical License (# MD036712) renewed every 2 years since

Boards, other specialty certification
2014-present Board Certified, American Board of Surgery #059069

Clinical (Service) Responsibilities
2014-present Faculty, Endocrine Surgery. Clinical activity 1.5 days/week
2017-present Director, Endocrine Surgery Fellowship Program

Clinical Productivity
2017-present My targeted clinical effort assignment is 25%. My wRVU target is 2150 and I have consistently
met or exceeded this target.

Clinical Draw from outside local/regional area
2014-present 20% of my patients came from other states such as DE, DC, FL, NY,OH, PA, SC, TN, VA, WV WV
International patients came from other countries such as Nigeria, Haiti, Bermuda, Middle East,
Honduras, and Pakistan.

Membership in or examiner for specialty board
None

Clinical Program Building / Leadership
2016- present Johns Hopkins Endocrine Surgery in the National Capitol Region at Sibley Memorial Hospital. I helped expand the JHUSOM Endocrine Surgery footprint to the NCR at Sibley. I helped to setup the endocrine surgery outpatient clinic including instrumentation and the operating rooms.

Clinical Demonstration Activities
None

Development of nationally/internationally recognized clinical standard of care
None

EDUCATIONAL ACTIVITIES

Educational Focus

My educational focus has centered around surgical management of thyroid, parathyroid, or adrenal disease. My target audiences are medical students, residents, and fellows by providing instruction in the operating room, clinics, classroom and anatomy labs. These activities include:

-Teaching thyroid and lateral Neck Anatomy (via cadavaeric dissection labs) to Residents

-Teaching residents and fellows (Endocrine and Surgical Oncology) surgical management of thyroid, adrenal,
and parathyroid disorders via lectures

- Friday morning Resident and Fellow Endocrine Surgery conference
- Resident and Surgical Oncology Fellow Oral Board Exam Preparation
- Medical student tumor board
- Medical student Professors Hours
- CME Instruction
- Capstone project mentor for MPH students at Johns Hopkins School of Public Health
- Faculty advisor for medical students
- Johns Hopkins Medical School Admissions Committee

Teaching

Classroom instruction

JHMI/Regional

2014-present	Facilitator for 3rd year medical students on surgery clerkship, Medical Student Tumor Board that convenes every other month
2014-present	Facilitator, weekly endocrine surgery conference for fellows, residents, and students on endocrine surgery service
2/5/2015	Educator; Resident cadaveric labs: head and neck dissection
2/11/2015	Resident Lecturer; Parotidectomy, Neck Dissection; Thyroid and Parathyroid Disease
2/19/2015	Resident Lecturer; Adrenal masses and adrenalectomy
2/26/2015	Educator; Resident cadaveric labs: head and neck dissection
11/19/2015	Resident Lecturer; Head and Neck Diagnosis, Oral cavity lesions, and neck masses
2/4/2016	Resident Lecturer; Adrenal masses and adrenalectomy
9/8/2016	Substitute Educator – Clinical Foundations Medicine Course SOM, 1st year medical student
10/13/2016	Resident Lecturer; Endocrine problems and work up
10/27/2016	Resident Lecturer; Endocrine problems and work up
12/15/2016	Educator; Resident cadaveric labs: head and neck dissection
11/2/2017	Resident Lecturer; Endocrine problems and work up
11/16/2017	Resident Lecturer; Neck masses
6/20/2018	Professors Hour with medical students
6/20/2018	Mock Interview night with medical students
9/26/2018	Facilitator, Medical Student Tumor board (3rd year medical students)
10/11/2018	Resident Lecturer; Endocrine Problems and work up Part 1
10/11/2018	*The Johns Hopkins University Interprofessional Education and Interprofessional Clinical Practice: SOM, SON, and Norte Dame of Maryland School of Pharmacy (SOP)* Selected SOM Faculty Mentor, IPE Event #1: Values and Ethics for Interprofessional Practice Curriculum, first year pre-licensure medical, nursing, and pharmacy learners

(~200 students) from JH School of Medicine, JH School of Nursing and the Notre Dame of Maryland University School of Pharmacy are required to participate in four IPE events during their studies as part of a graduation requirement from each of the respective programs.

10/18/2018 Resident Lecturer; Endocrine Problems and work up Part II

10/3/2019 Resident Lecturer; Thyroid

10/10/2019 *The Johns Hopkins University Interprofessional Education and Interprofessional Clinical Practice: SOM, SON, and Norte Dame of Maryland School of Pharmacy (SOP)*
Selected SOM Faculty Mentor, IPE Event #1: Values and Ethics for Interprofessional Practice Curriculum, first year pre-licensure medical, nursing, and pharmacy learners (~200 students) from JH School of Medicine, JH School of Nursing and the Notre Dame of Maryland University School of Pharmacy are required to participate in four IPE events during their studies as part of a graduation requirement from each of the respective programs.

1/21/2020 *The Johns Hopkins University Interprofessional Education and Interprofessional Clinical Practice: SOM, SON, and Norte Dame of Maryland School of Pharmacy (SOP)*
Selected SOM Faculty Mentor, IPE Event #3: Values and Ethics for Interprofessional Practice Curriculum, first year pre-licensure medical, nursing, and pharmacy learners (~200 students) from JH School of Medicine, JH School of Nursing and the Notre Dame of Maryland University School of Pharmacy are required to participate in four IPE events during their studies as part of a graduation requirement from each of the respective programs.

10/21/2020 IPE Events Values and Ethics for Interprofessional Practice

- Professionalism for Nursing in Health Care: With Hopkins Nursing Seminar-Ethics and Cultural
  - Humility (SON: 120.501)
- SOM requirement
- SOP requirement

2/2/2021 Surgical Oncology Fellow Mock Oral Boards

2/9/2021 IPE Event#4 Values and Ethics for Interprofessional Practice: Communication and Teamwork

- Professionalism for Nursing in Health Care: With Hopkins Nursing Seminar-Ethics and Cultural
  - Humility (SON: 120.501)
- SOM requirement
- SOP requirement

2/11/2021 Resident Lecture, Endocrine Problems I

National None
International None

Clinical instruction
JHMI/Regional
2014-present Attending Surgeon, 3rd year med students, residents and fellows, operating room weekly

National None
International None

CME instruction
JHMI/Regional
10/2/2015 Speaker, "Medullary Thyroid Cancer," and Panelist "Management of the Thyroid Nodule" Contemporary Surgical Management of Thyroid and Parathyroid Disease, The Johns Hopkins Hospital
11/18/2016 Speaker, "Medullary Thyroid Cancer," and Panelist "Management of the Thyroid Nodule" Contemporary Surgical Management of Thyroid and Parathyroid Disease, The Johns Hopkins Hospital
11/17/2017 Speaker, "Medullary Thyroid Cancer," and Panelist "Management of the Thyroid Nodule" Contemporary Surgical Management of Thyroid and Parathyroid Disease, The Johns Hopkins Hospital
11/9/2018 Speaker, "Medullary Thyroid Cancer," and Panelist "Management of the Thyroid Nodule" Contemporary Surgical Management of Thyroid and Parathyroid Disease, The Johns Hopkins Hospital
6/19/2019 Speaker, "Surgical Approaches to Adrenal Disease" Inaugural Case Based Issues in Adrenal Disorders: Case-based Management, The Johns Hopkins Hospital
11/22/2019 Speaker, "Medullary Thyroid Cancer," and Panelist "Management of the Thyroid Nodule" Contemporary Surgical Management of Thyroid and Parathyroid Disease, The Johns Hopkins Hospital

National None
International None

Workshops /seminars
JHMI/Regional None
National None
International None

Mentoring
Pre-doctoral Advisees /Mentees
2017- 2019 Lindsay Dickerson, medical student, now a general surgery resident at University of Washington
2017- 2019 Sophie Lin, medical student, now in residency
2017 – 2018 Fadi Murad
MPH student for Capstone Project
Mentor on poster 10/18

2016-2017 Ghedak Ansari
MPH student for Capstone Project
Mentor on publication OR[22]

2016-2017 Ashwyn Sharma, medical student
Current Surgical Resident at UCSD
Mentor on publication CR[2]

2014- 2016 Neeraja Nagarajan, MD MPH
Presently working at McKinsey Consulting
Mentored publication OR [18]

Post-doctoral Advisees /Mentees

2020-Present Shkala Karzai, MD
Endocrine Surgery Fellow
Mentor on OR [36,37]

2019-Present Whitney Sutton, MD
General Surgery Resident
Mentor on OR [29-31, 35-37] and Poster 10/19

2018–2019 Jessica B. Shank, MD
Endocrine Surgery Fellow
Mentor on publication RA[5] and poster 8/19

2018-2019 Sandra DiBrito, MD
General Surgery Resident
Mentor on publication OR[28]

2017-2018 Said Azoury, MD
General Surgery Resident
Mentored publication BC[7]

2016-2018 Zeyad Sahli, MD
Presently general surgery resident at UVA
Received American Thyroid Association trainee grant
Mentored publications OR[19-24,33,34] and CR[1]

2014-2015 Stacie Kahan, MD
Endocrine Surgery Fellow
Mentored publication OR[18]

Thesis committees
None

Educational Program Building / Leadership
2017 – Present Endocrine Surgery Fellowship Program Director, Johns Hopkins University School of Medicine.

In my capacity, I am responsible for the oversight and training experience that fulfills the requirements of the accrediting society to one Endocrine Surgery Fellow per year. I also maintain accreditation for our fellowship program.

Educational Demonstration Activities to external audiences, on or off campus
None

RESEARCH ACTIVITIES

Research Focus
I am a board-certified general surgeon and a fellowship-trained endocrine surgeon with multiple years of research experience beginning at the National Cancer Institute. My previous and current research has focused on improving the care and outcomes of patients with diseases of the thyroid, parathyroid, and adrenal glands. My current focus is on understanding outcomes in older adults. I am also obtaining advanced training at the Bloomberg School of Public Health to better position myself to perform high quality research. Ultimately, I hope to become an independent R01 funded investigator and leader in the field of endocrine surgery clinical outcomes research.

Research Program Building / Leadership
None

Research Demonstration Activities
None

Inventions, Patents, Copyrights
None

Technology Transfer Activities
None

SYSTEM INNOVATION AND QUALITY IMPROVEMENT ACTIVITIES
System Innovation Focus
My primary system innovation focus has centered around improving patient safety and quality. As a physician champion of Enhanced Recovery after Surgery (ERAS), my goal was to coordinate and standardize patient discharge after thyroidectomy across multiple disciplines at Johns Hopkins Hospital. As the Site Director of Collaborative Endocrine Surgery Quality Improvement Program (CESQIP), my goal is to incorporate Johns Hopkins endocrine surgical outcomes within this national database to ultimately help us improve quality of care and outcomes for our patients.

System Innovation and Quality Improvement efforts within JHMI:

1/2015-1/2016	Physician Champion, Enhanced Recovery After Surgery (ERAS) Thyroid Clinical Pathway. surgeon representative to create a standard pathway for early and safe discharge after thyroid surgery
10/2017 - present	Physician Champion, Comprehensive Unit-based Safety Program (CUSP) in The Johns Hopkins Outpatient Center Operating Room (JHOC OR). Responsible for representing surgeons perspective as well as serving as a liaison to address any safety concerns and ensure safe care in the JHOC OR.

7/2020 – present Site Director, Collaborative Endocrine Surgery Quality Improvement Program (CESQIP). This is a national quality improvement registry founded by members of the American Association of Endocrine Surgeons that collects data on endocrine surgical procedures.

System Innovation and Quality Improvement efforts outside of JHMI:
None

System Innovation and Quality Improvement Program Building/Leadership:
None

ORGANIZATIONAL ACTIVITIES

Institutional Administrative Appointments
2017- present Member, Compensation Committee Department of Surgery
2017- present Physician Champion, JHOC CUSP Committee
2018- present Member, Department of Surgery Employee Recognition Committee
2020- present Member, Johns Hopkins University School of Medicine Admissions Committee
2021- present Co-Director, Women in Surgery at Hopkins (WISH)
2021- present Co-Director, Johns Hopkins Thyroid Tumor Center

Editorial Activities
None

Editorial Board appointments
2020-present Member, Editorial Board, *Frontiers in Endocrinology*
2020-present Member, Editorial Board, *Thyroid*

Journal peer review activities
2016-present *Thyroid*
2016-present *World Journal of Surgery*
2017-present *Surgery*
2018-present *American Journal of Surgery*
2018-present *British Medical Journal Case Reports*
2018-present *Journal of Surgical Research*
2019-present *BMC Cancer Journal*

Other peer review activities
None

Advisory Committees, Review Groups/Study Sections
2017 – present Invited Member, ECOG-ACRIN National Surgery Committee
2019 – present Selected Early Career NIH Study Section Program Member (Invitations to be ad hoc NIH Study section member for NIH grants)
6/2019 Invited NCI Study Section Member, Clinical Oncology Study Section (CONC) Denver, CO, June 17-18, 2019.
2/2021 Invited Member, NIA Research Centers Collaborative Network Inclusion of Older Adults in Clinical Studies

Professional Societies

2010-present American Association of Endocrine Surgeons
- 2010-present Member
- 2017-present Collaborative Endocrine Surgery Quality Improvement Program (CESQIP) Committee
- 2017-present Fellowship Committee

2013-present American Thyroid Association
- 2013-present Member
- 2019-present Trainees and Career Advancement Committee
- 2020-present Research Evaluation Taskforce

2015-present Association of Women Surgeons
- 2015-present Member
- 2019-present Institutional membership committee

2015-present Member, American Association of Clinical Endocrinologists

2015-present Fellow, American College of Surgeons
- 2020-present Geriatric Surgery Verification Task Force

2016-present Member, American Association of Academic Surgeons

Member, Endocrine Society

2018-present Member, Society of Asian Academic Surgeons

Conference Organizer

JHMI/Regional

11/9/2018 Conference Co-Director Contemporary Surgical Management of Thyroid and Parathyroid Disease, The Johns Hopkins Hospital

11/22/2019 Conference Co-Director Contemporary Surgical Management of Thyroid and Parathyroid Disease, The Johns Hopkins Hospital

National None

International None

Session Chair

JHMI/Regional

None

National

4/9/2019 Session Chair, American Association of Endocrine Surgeons, Annual Meeting, Los Angeles, CA

9/26/2019 Session Chair, Society of Asian Academic Surgeons, Annual Meeting, Boston, MA

International

8/13/2019 Session Chair, International Association of Endocrine Surgeons Meeting, Annual Meeting, Krakow, Poland

Consultantships

None

RECOGNITION

Awards, Honors

2010 American Association of Endocrine Surgeons, Best Clinical Poster Award
2010 Charles A. Hufnagel Award for Excellence in Basic Science Research,
2011 Marie J. Simonian Award for Excellence in Clinical Research
2012 String of Pearls Teaching Award Nominee
2013 American Thyroid Association Training Grant
2018 Selected as a Johns Hopkins School of Medicine Interprofessional Collaborative Practice Physician Exemplar (faculty representing the field of medicine in healthcare as a physician role model for pre and post licensure learners in nursing, medicine, pharmacy and public health; 23 institutionally selected)
2019 Selected as a Johns Hopkins School of Medicine Interprofessional Collaborative Practice Physician Exemplar (faculty representing the field of medicine in healthcare as a physician role model for pre and post licensure learners in nursing, medicine, pharmacy and public health; 23 institutionally selected)
2019 Invited abstract judge for the 2020 Medical Student Research Symposium
2020 Selected as a Johns Hopkins School of Medicine Interprofessional Collaborative Practice Physician Exemplar (faculty representing the field of medicine in healthcare as a physician role model for pre and post licensure learners in nursing, medicine, pharmacy and public health; 23 institutionally selected)

Invited Talks

JHMI/Regional

12/2014 Speaker, Surgical Grand Rounds, Sibley Memorial Hospital "Thyroid Surgery in the Era of Molecular Markers," Washington DC
11/2015 Speaker, Center of Older Americans Independence Center "Thyroid Gland and Frailty" Baltimore, MD
11/2016 Speaker, Contemporary Surgical Management of Thyroid and Parathyroid Disease "Medullary Thyroid Cancer", Baltimore, MD
11/2018 Speaker, Contemporary Surgical Management of Thyroid and Parathyroid Disease "Medullary Thyroid Cancer" Baltimore, MD
11/2019 Speaker, Contemporary Surgical Management of Thyroid and Parathyroid Disease "Medullary Thyroid Cancer"
9/20/2019 Speaker, The Johns Hopkins Inaugural Contemporary Issues in Adrenal Disorders CME "Surgical Approaches to Adrenal Disease" Baltimore, MD
1/18/2020 Speaker, The American College of Surgeons Metropolitan DC Chapter "Endocrine Surgery Absite Review" Fairfax, VA
4/2/2020 Speaker, Surgical Grand Rounds, The Johns Hopkins Hospital "Ageism and Thyroid Surgery" Baltimore, MD

National

6/2016 Speaker, Premier National Meeting, "Leveraging Patient Care Using the Premier Database"
Washington, DC

12/15/2020 Invited Speaker, Georgetown Medstar Surgical Outcomes Club, "Ageism in Endocrine Surgery"

International None

Visiting Professorships
None

OTHER PROFESSIONAL ACCOMPLISHMENTS

Posters

4/10 **Aarti Mathur**, Mahadev Rao, Yuwei Zhang, Mary Zhang, Clint D. Kemp, Robert T. Ripley, Julie Hong, Fang Liu, Itzhak Avital, David S. Schrump. "Cigarette smoke induces expression of the putative stem cell marker ABCG2 in cultured esophageal adenocarcinoma cells." American Association for Cancer Research Annual Meeting, Washington, D.C.

4/10 **Aarti Mathur**, Clinton D. Kemp, Utpal Dutta, Smita Baid, Alejandro Ayala, Richard E Chang, Seth Steinberg, Eileen Lange RN, James F. Pingpank, H. Richard Alexander, W. Marston Linehan, Peter A. Pinto, Giao Phan, Marybeth Hughes, Steven K. Libutti, Constantine Stratakis, Electron Kebebew. "Adrenal Venous Sampling in Primary Hyperaldosteronism: Standardizing a Gold Standard." American Association of Endocrine Surgeons Annual Meeting, Pittsburgh, PA

10/16 **Mathur A**, Nagarajan N, Kahan S, Schneider EB, Zeiger MA. "Association of parathyroid hormone level with post-thyroidectomy hypocalcemia: A systematic-review." American Thyroid Association Annual Meeting, Denver, Colorado.

4/17 Sahli Z, Najafian A, Kahan S, Schneider EB, Zeiger MA, **Mathur A**. "One-hour postoperative parathyroid hormone levels do not reliably predict hypocalcemia after thyroidectomy." American Association of Endocrine Surgeons Annual Meeting, Orlando, FL.

10/17 Sahli Z, Canner JK, Najjar O, Schneider EB, Prescott JD, Russell JO, Tufano RP, Zeiger MA, **Mathur A**. "The Association between Age and Patient-reported Changes in Voice and Swallowing after Thyroidectomy." American Thyroid Association Annual Meeting, Victoria, BC, Canada.

10/18 Murad F, Canner JK, Haut E, Prescott JD, Segev DL, Zeiger MA, **Mathur A.** "The Epidemiology of Thyroid Cancer in Older Adults." American Thyroid Association Annual Meeting, Washington DC.

8/19 Shank JB, Alkahili E, Canner JK, Hamrahian A, Munir M, Salvatori R, Prescott JD, **Mathur A**. "Unilateral adrenalectomy as initial management of Cushing's syndrome secondary to bilateral macronodular hyperplasia." International Association of Endocrine Surgeons Meeting, Krakow Poland.

10/19 Sutton W, Canner JK, Segev DL, Zeiger MA, **Mathur A**. "Differentiated thyroid cancer in older adults: Does a treatment disparity still exist?" American Thyroid Association Annual Meeting, Chicago, IL.

Oral/Podium Presentations

4/2010 **Aarti Mathur**, Julie Weng , Willieford Moses , Seth Steinberg, Quan-Yang Duh, Orlo H. Clark, Electron Kebebew. "A prospective trial evaluating the accuracy of using combined clinical factors and candidate diagnostic markers to refine the accuracy of thyroid fine needle aspiration biopsy." American Association of Endocrine Surgeons Annual Meeting, Pittsburgh, PA.

4/14 **Aarti Mathur**, Alireza Najafian, Eric B. Schneider, Martha A. Zeiger, Matthew T. Olson. "Malignancy risk and reproducibility associated with atypia of undetermined significance on thyroid cytology." American Association of Endocrine Surgeons Annual Meeting, Boston, MA.

4/15 Noureldine SI, Najafian A, Aragon Han P, Olson MT, Genther DJ, Schneider EB, Prescott JD, Agrawal N, **Mathur A**, Zeiger MA, Tufano RP. "Evaluation of the effect of diagnostic molecular testing on the surgical decision-making process for patients with thyroid nodules". American Association of Endocrine Surgeons Annual Meeting, Nashville, TN. [Dr. Noureldine gave the talk]

4/17 Karipineni F, Sahli Z, Somervell H, **Mathur A**, Prescott JD, Tufano RP, Zeiger MA. "Are preoperative sestamibi scans useful for identifying ectopic parathyroid glands in patients with expected multigland parathyroid disease?" American Association of Endocrine Surgeons Annual Meeting, Orlando, FL. [Dr. Karipineni gave the talk]

10/18 Sahli ZT, Ansari G, Gurakar M, Canner JK, Segev D, Zeiger MA, **Mathur A**. "Thyroidectomy in older adults: an ACS-NSQIP study of outcomes." Association of Academic Surgery Annual Meeting, Jacksonville, FL [Dr. Sahli gave the talk]

5/18 Sahli ZT, Karipineni F, Hang, Canner JK, **Mathur A**, Prescott JD, Sheth S, Ali SZ, Zeiger MA. "The Association between Ultrasonography TIRADS Classification System and Surgical Pathology Among Indeterminate Thyroid Nodules." American Association of Endocrine Surgeons Annual Meeting, Durham, NC

4/20 Sutton W, Genberg B, Prescott JD, Segev DL, Zeiger MA, Bandeen-Roche K, **Mathur A**. Understanding Surgical Decision-Making in Older Adults with differentiated thyroid cancer: A discrete choice experiment.

American Association of Endocrine Surgeons Annual Meeting, Birmingham, AL. Meeting cancelled

2/21 Sutton W, Ahn JB, Prescott JD, Zeiger MA, Segev DL, McAdams-DeMarco M, **Mathur A**. Association between treatment of secondary hyperparathyroidism and post-transplant outcomes. Academic Surgical Congress [Dr. Sutton gave the talk]

Military Service

None

Community Services

None

Humanitarian Activities

None

Philanthropic Activities

None

Other

None

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Mathur, Aarti

eRA COMMONS USER NAME (credential, e.g., agency login): amathu10

POSITION TITLE: Associate Professor of Surgery

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
University of Texas, Austin, TX	B.A.	08/1996	05/2000	Biochemistry
University of Texas Medical Branch, Galveston, TX	M.D.	08/2000	05/2004	Medicine
Georgetown University Hospital, Washington, DC		07/2004	06/2005	Intern, General Surgery
Georgetown University Hospital, Washington, DC		07/2005	06/2007	Residency, General Surgery
The National Cancer Institute, Bethesda, MD		07/2007	06/2011	Research & Clinical Fellow Surgical Oncology
Georgetown University Hospital, Washington DC		07/2011	06/2013	Residency, General Surgery
The Johns Hopkins Hospital Baltimore, MD		07/2013	06/2014	Fellowship, Endocrine Surgery
The Johns Hopkins Bloomberg School of Public Health	Ph.D	06/2017		Graduate Training in Clinical Investigation

A. Personal Statement

I am a board-certified general surgeon and a fellowship-trained endocrine surgeon with multiple years of research experience applying for the Atterbury Family Foundation Discovery Grant. My primary clinical and research interests are focused on improving the care and outcomes of older patients with thyroid cancer. My motivation to better understand the decision-making process in managing endocrine surgical diseases in older adults stems from my interactions with patients and their treatment failures. I am currently funded by an NIA K23 Mentored Career Development Award to study the association between frailty with post-operative changes in voice, swallowing, and quality of life following thyroidectomy in older adults. Over the past 3 years, I have published multiple manuscripts examining how age and frailty affect post-surgical outcomes in older adults (Contribution 1). I have also started to understand the decision-making process in managing well differentiated thyroid cancer in older adults (Contribution 2). In addition, I have also completed advanced coursework in Clinical

Investigation for the Johns Hopkins Bloomberg School of Public Health that will lead to a PhD this year.

Although I have previously studied decision making from the eyes of surgeons, this proposal will focus on patient centered decision making with the goal of improving risk stratification and prognostication to develop a personalized approach to treatment of older patients with thyroid cancer. The ultimate goal of this work is to generate preliminary data for submission on an NIH R01 grant as a New/Early stage investigator.

B. Positions and Honors

Positions and Employment

2004-2005 Internship, Department of General Surgery, Georgetown University, Washington, DC

2005-2007 Residency, Department of General Surgery, Georgetown University, Washington, DC

2007-2011 Fellowship, National Cancer Institute/Surgical Oncology National Institute of Health
Bethesda, MD

2011-2013 Residency, Department of General Surgery, Georgetown University, Washington, DC

2013-2014 Fellowship, Endocrine Surgery, The Johns Hopkins University, Baltimore, MD

2014-2020 Assistant Professor, Department of Surgery, The Johns Hopkins University School of Medicine,
Baltimore, MD

2020-present Associate Professor, Department of Surgery, The Johns Hopkins University School of Medicine,
Baltimore, MD

Other Experience and Professional Memberships

2007- District of Columbia Medical License
2010- Member, American Association of Endocrine Surgeons
2013- Member, American College of Surgeons
2014- State of Maryland Medical License
2014- Board Certified, American Board of Surgery
2014- Member, American Thyroid Association
2014- Member, Association of Women Surgeons
2017- Fellow, American College of Surgeons

Honors

2010 American Association of Endocrine Surgeons Poster Competition Award
2010 Charles A. Hufnagel Award for Excellence in Basic Science Research
2011 Marie J. Simonian Award for Excellence in Clinical Research
2012 String of Pearls Teaching Award Nominee

2013	American Thyroid Association Training Grant
2015	The Johns Hopkins Department of Surgery Rothman Research Award
2016	The Johns Hopkins Clinician Scientist Award

C. Contributions to Science

1. Effects of Aging on Thyroid Cancer Diagnosis and Management

One of my primary research interests is endocrine surgical outcomes in older adults, specifically thyroid cancer. I have focused on understanding how age and frailty affect outcomes after thyroidectomy. We have demonstrated that older adults can have self-reported changes in voice and swallowing after thyroidectomy. Additionally, older adults can have worse clinical outcomes after thyroidectomy.

a. Sutton W, Canner JK, Rooper LM, Prescott JD, Zeiger MA, **Mathur A**. Is patient age associated with risk of malignancy in a ≥4cm cytologically benign thyroid nodule? The Am J of Surg. 2020, June 2. PMID: 32532458; NIHMS ID: NIHMS1603450
b. Sahli ZT, Canner JK, Najjar O, Schneider EB, Prescott JD, Russell JO, Tufano RP, Zeiger MA, **Mathur A**. Association between age and patient-reported changes in voice and swallowing after thyroidectomy. Laryngoscope. 2019; 129(2):519-524. PMCID: PMC6344315
c. Sahli ZT, Zhou S, Najjar O, Onasanya O, Segev DL, Massie A, Zeiger MA, **Mathur A**. Octogenarians have worse clinical outcomes after thyroidectomy. Am J Surg. 2018; 216(6):1171-1176. PMCID: PMC6197934
d. Sahli ZT, Ansari G, Gurakar M, Canner JK, Segev DL, Zeiger MA, **Mathur A**. Thyroidectomy in older adults: an ACS-NSQIP study of outcomes. J Surgical Research. 2018; 229:20-27. PMCID: PMC6042653

2. Treatment Variation and Surgical Decision-Making in Older Adults with Thyroid Cancer

Another area of focus as a surgeon has been understanding treatment variations for thyroid cancer and decision making in older adults. We were one of the first groups in the country to perform a discrete choice experiment to understand surgical decision making in older adults with differentiated thyroid cancer. We have also shown that significant treatment variations exist in managing older adults with thyroid cancer.

a. Sutton W, Canner JK, Segev DL, Zeiger MA, **Mathur A**. Treatment variation in older adults with differentiated thyroid cancer. J Surg Research. 2020; 254:154-164. PMCID: PMC7483795
b. Noureldine SI, Najafian A, Aragon Han P, Olson MT, Genther DJ, Schneider EB, Prescott JD, Agrawal N, **Mathur A**, Zeiger MA, Tufano RP. Evaluation of the effect of diagnostic molecular testing on the surgical decision-making process for patients with thyroid nodules. JAMA Otolaryngol Head Neck Surg. 2016; Jul 142(7): 676-82. PMID: 27196108; NIHMS ID: NIHMS1584523

3. Improving outcomes in patients with hyperparathyroidism.

Another area of research focus is understanding how to optimize diagnostic and surgical outcomes for patients with hyperparathyroidism. We have studied optimizing parathyroid hormone levels in addition to sestamibi imaging to achieve better ultimate outcomes for patients.

a. Sahli ZT, Najafian A, Kahan S, Schneider EB, Zeiger MA, **Mathur A**. One-hour postoperative parathyroid hormone levels do not reliably predict hypocalcemia after thyroidectomy. World J Surg. 2018; 42(7): 2128-2133. PMCID: PMC5991999
b. **Mathur A**, Nagarajan N, Kahan S, Schneider EB, Zeiger MA. Association of parathyroid hormone level with post-thyroidectomy hypocalcemia: A systematic-review. JAMA Surgery. 2018; 153(1):69-76. PMID: 29167863
c. Trinh G, Rettig E, Noureldine SI, Russell JO, Agrawal N, **Mathur A**, Prescott JD, Zeiger MA, Tufano RP. Surgical management of normocalcemic primary hyperparathyroidism and the impact of intraoperative parathyroid hormone testing on outcome. Otolaryngol Head Neck Surg. 2018; 159(4): 630-637. PMID: 30105919
d. Karipineni F, Sahli Z, Somervell H, **Mathur A**, Prescott JD, Tufano RP, Zeiger MA. Are preoperative sestamibi scans useful for identifying ectopic parathyroid glands in patients with expected multigland parathyroid disease? Surgery. 2018; 163(1):35-41. PMID: 29154082

4**. Thyroid gland and molecular testing to identify thyroid cancer**

My focus on the thyroid gland involved refining the accuracy of fine-needle aspiration biopsy for an indeterminate thyroid nodule using molecular markers or second review of cytology. To support the use of molecular markers, we discovered an increasing prevalence of BRAF mutation over time in papillary thyroid carcinomas.

a. **Mathur A**, Weng J, Moses W, Steinberg SM, Rahbari R, Kitano M, Khanafshar E, Ljung B, Duh Q, Clark OH, Kebebew E. A prospective trial evaluating the accuracy of using combined clinical factors and candidate diagnostic markers to refine the accuracy of thyroid fine needle aspiration biopsy. *Surgery* 2010. Dec; 148(6): 1170-6. PMCID: PMC3052943
b. **Mathur A**, Moses W, Rahbari R, Khanafshar E, Duh QY, Clark O, Kebebew E. Higher Rate of BRAF mutation in papillary thyroid cancer over time: A single-institution study. *Cancer* 2011: Oct; 117(19):4390-5. PMID: 21412762
c. **Mathur A**, Najafian A, Schneider EB, Zeiger MA, Olson MT. Malignancy risk and reproducibility associated with atypia of undetermined significance on thyroid cytology. Surgery 2014: Dec 156(6): 1471-6. PMID: 25218896
d. Rahbari R, **Mathur A**, Kitano M, Guerrero M, Shen WT, Duh Q, Clark OH, Kebebew E. Prospective randomized trial of ligasure versus harmonic hemostasis technique in thyroidectomy. *Annals of Surgical Oncology* 2011 Apr; 18(4): 1023-7. PMID: 21072688

5. Gene therapy and stem cell markers

My initial publications involved translational basic science to incorporate gene therapy and stem cell markers in treating various malignancies. I was initially involved in studying the role of adoptive cell transfer and the timing of surgical treatment in metastatic melanoma. After treating patients with human and mouse T-cells targeted to specific melanoma antigens, we observed tumor responses in patients with metastatic melanoma. We then studied the role of metastasectomy and found that it could prolong survival in a select group of patients. These concepts were then expanded to metastatic pancreatic cancer, lung, and esophageal cancer.

37. Johnson LA, Morgan RA, Dudley ME, Cassard L, Yang JC, Hughes MS, Kammula US, Royal RE, Sherry RM, Wunderlich JR, Lee CC, Restifo NP, Schwarz SL, Cogdill AP, Bishop RJ, Kim H, Brewer CC, Rudy SF, VanWaes C, Davis JL, **Mathur A**, Ripley RT, Nathan DA, Laurencot CM, Rosenberg SA. Gene Therapy with human and mouse T-cell receptors mediates cancer regression and targets normal tissues expressing cognate antigen. *Blood* 2009 Jul 16; 114(3): 535-46. PMCID: PMC2929689
38. Ripley RT, Davis JL, Klapper JA, **Mathur A**, Kammula U, Royal RE, Yang JC, Sherry RM, Hughes MS, Libutti SK, White DE, Steinberg SM, Dudley ME, Rosenberg SA, Avital I. Liver Resection for Metastatic Melanoma with Postoperative Tumor-Infiltrating Lymphocyte Therapy. *Ann Surg Oncol* 2010 January; 17: 163-170. PMCID: PMC6292221
39. Royal RE, Levy C, Turner K, **Mathur A,** Hughes M, Kammula US, Sherry RM, Topalian SL, Yang JC, Lowy I, Rosenberg SA. Phase 2 trial of single agent Ipilimumab (anti-CTLA-4) for locally advanced or metastatic pancreatic adenocarcinoma. *J Immunotherapy* 2010; Oct 33(8): 828-33. PMCID: PMC7322622
40. Zhang M, **Mathur A**, Zhang Y, Xi S, Atay S, Hong JA, Datrice N, Upham T, Kemp CD, Ripley RT, Wiegand G, Avital I, Fetsch P, Mani H, Zlott D, Robey R, Bates SE, LI x, Rao M, Schrump DS. Mithramycin represses basal and cigarette smoke-induced expression of ABCG2 and inhibits stem cell signaling in lung and esophageal cancer cells. Cancer Res 2012. Aug; 72(16); 4178-92. PMCID: PMC6261440

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support
2017/04/01 – 2022/03/31
K23AG053429
Mathur, Aarti (PI)
Association between Frailty and Post-thyroidectomy Alterations in Voice, Swallowing, and Quality of Life.
The aims of this project are to quantify voice, swallowing, and quality of life outcomes in patients who undergo
thyroid surgery, and to assess the association between frailty and those changes.
Role: PI

2021/01/01 – 2022/01/01
Atterbury Thyroid Tumor Center Foundation
Mathur, Aarti (PI)
Understanding Decision-making in older patients with thyroid cancer
The aims of this project are to use qualitative methods to understand how referring providers and surgeons make decisions to refer patients.
Role: PI

Completed Research Support
2015/08/01 – 2017/07/31
Older Americans Independence Center Pilot/Exploratory Studies Core Award
Mathur, Aarti (PI)
Alterations in voice and swallowing after thyroidectomy
The goal of this pilot is to explore the prevalence of alterations in voice and swallowing in older individuals undergoing thyroidectomy.
Role: PI

2016/01/01-2017/01/01
Rothman Pilot Award
Mathur, Aarti (PI)
Outcomes after thyroidectomy in older adults
The goal of this pilot study is to explore outcomes after thyroidectomy in older adults.
Role: PI

2016/01/01- 2018/01/01
Johns Hopkins Clinician-Scientist Award
Mathur, Aarti (PI)
Association between frailty and outcomes after thyroidectomy
The goal of this pilot is to explore the prevalence of alterations in voice and swallowing in older individuals undergoing thyroidectomy and the ability of frailty to predict these alterations.
Role: PI